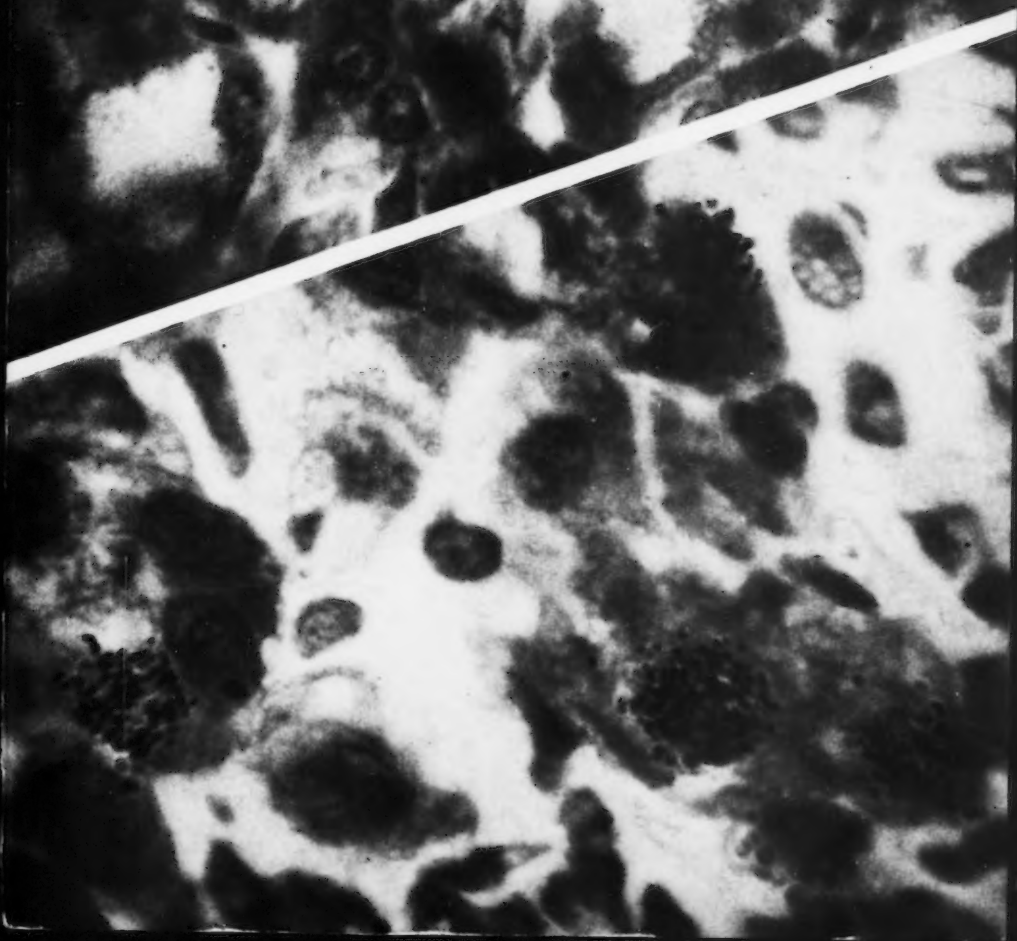


September-October 1958 Vol. 8 No. 5 • Published by the American Cancer Society

CA

*Bulletin of
Cancer Progress*



*"every little bit
added to what
you got makes just
a little bit more"*

The use of X rays is one of the most important assets of modern medicine. Practice without it would be greatly handicapped. Yet, it has been long recognized that large doses of X ray and other ionizing radiations can be often harmful. Some recent studies indicate that even very small doses of radiation may not always be completely harmless. It is still not certain whether any possibility of harm exists at the very low levels of radiation exposure encountered in diagnostic X-ray procedures, but until the matter can be conclusively settled we must assume that it may.

It is important for doctors to recognize that any unnecessary radiation exposure is undesirable, because it is possible to reduce radiation exposure without losing any of the priceless benefits of X ray in medical practice. Our own observations, confirmed by recent surveys in several communities, indicate that large reductions in the radiation exposure of patients can be made by greater attention, on the part of doctors using X-ray apparatus, to the fine points of radiographic technique. The proper use of cones, filters and kilovoltage is particularly important. Further reductions can be achieved by the substitution of radiography for fluoroscopy (fluoroscopy generally entails greater radiation exposure) whenever it can be done without loss of needed diagnostic information. I have seldom seen doctors use radiation indiscriminately or without good indication, but I have seen a number of doctors who were not aware of the bargains that can be obtained in reduced exposure by the use of the best modern equipment and techniques.

Eugene P. Rindgraves

Vice-President and President-Elect
American Cancer Society

Cover—

Top: Autoradiogram of NORMAL rat pancreas. Dots over the *nucleolus* are grains of photographic emulsion above the tissue which indicate the presence of radioactivity in this distinct structure of the nucleus. The *nucleolus* plays a significant part in the ribonucleic acid (RNA) metabolism and, possibly, in protein synthesis of the cell. Cytidine—a nucleic acid precursor—was labeled with tritium (H^3 , the radioactive isotope of hydrogen) and injected into the animal which was sacrificed 30 minutes later. The concentration of the isotope in the *nucleolus* indicates a rapid rate of synthesis of RNA in this cytologic structure. ($\times 850$)

Bottom: Autoradiogram of REGENERATING rat pancreas. Grains of photographic

emulsion over the nuclei indicate the presence of tritium (H^3) diffusely scattered throughout the *nucleus*. Thymidine, a deoxyribonucleic acid (DNA) precursor, labeled with tritium, was injected into the animal, and shows incorporation into the chromatin (genes and chromosomes) of the *nucleus* 30 minutes after injection of the compound. Other autoradiograms indicate that thymidine was not concentrated in the *nucleolus*. ($\times 650$)

Thus with tritium-labeled nucleic acid precursors one may study the RNA metabolism of the nucleolus and the DNA metabolism of the nucleus of individual cells. Such an approach to cellular metabolism promises to add information to our knowledge of cell function—normal and abnormal. (See page 170.)

NEWSLETTER

SEPTEMBER-OCTOBER, 1958

FROM THE ROCKY MOUNTAIN CANCER CONFERENCE
DENVER, July 9-10, 1958

Jewett (Johns Hopkins) appealed for conservatism in treating cancer of the urinary bladder -- "it is not readily expendable, and its sacrifice imposes certain restrictions and alterations to life." He asked for accurate distinction between cases requiring and those not requiring radical cystectomy; and he urged family physicians to insist on immediate definitive diagnosis in the presence of hematuria and bladder irritability. In prostatic cancer, he said, it is advisable to withhold endocrine therapy until it is needed; castration is not indicated as a rule in early cases.

Macdonald (U. So. Calif.) gave these three rough categories in breast cancer: 1) the neoplasm pursues an orderly sequential course, in which time and the extent of the disease are related -- early diagnosis and adequate treatment are all important; 2) cases of doubtful operability -- "the clinician's most difficult problem" -- radiosensitivity usually indicates incurability; and 3) disseminated metastases -- only some receive palliation from steroidal therapy. He said that "the commendable effort to treat lumps of the breast early is a mixed blessing" and appealed for conservatism and nonmutilation until pseudolumps and lumps commonly involved in menstrual cycles are ruled out.

Rappaport (Chicago Medical School) reported that all myeloproliferative diseases have in common a progressive and usually irreversible proliferation of one or more of the marrow cellular constituents. Among these diseases, believed to stem from undifferentiated multipotent mesenchymal cells, are granulocytic leukemia, erythroleukemia, erythremic myelosis, polycythemia vera, megakaryocytic myelosis, idiopathic thrombocytopenia and myelofibrosis. One form of the disease may progress into another. He reported that lymph nodes enlarge often -- usually as a consequence of local or systemic infection. Persistently enlarged nodes should be biopsied; and if the node is to be removed, it should come out intact, capsule and all.

Samp (U. of Wis.) called attention to the procedure

of Mohs (also U. of Wis.) for the removal of suspicious or potentially troublesome moles. This is a combination of surgery and chemosurgery, accompanied by painstaking serial biopsies -- a procedure which has yielded excellent cure rates and cosmetic effects in the treatment of superficial cancers. . . . A principal problem in increasing cure rates is to induce reluctant patients to call their symptoms to the physician's attention and to return for follow-ups after treatment. . . . Many seemingly innocent conditions are worthy of the pathologist's attention: A pimple removed for cosmetic reasons turned out to be a carcinoma; a sebaceous cyst interfering with a baseball player's pitching was an adenocarcinoma; the lump which appeared on the sternum of a dieter who had succeeded in shedding much weight was a chondrosarcoma.

Karnofsky (Memorial, New York City) reported that a growing assortment of palliative preparations now can be offered the inoperable cancer patient. Radiomimetic drugs (e.g., HN2) should be administered with the close cooperation of the radiotherapist.

Altemeier (U. of Cincinnati) said that cancer of the biliary tree may be extrahepatic, intrahepatic or cholecystic and is difficult to treat. Some cases may be related to chronic infection and lithiasis.

Chamberlain (U. of Pa.) reported that one should take 4 to 5 minutes, rather than 4 to 5 seconds, to examine the neck properly for lumps. The exploring finger often is more useful than any other diagnostic measure in searching for oral tumors; and sometimes it is worthwhile extending it far down the throat, even if anesthesia must be employed. Cobalt bombs and isotopes can't be shown to have cured a single patient who wouldn't probably have responded equally well to conventional X rays. The new modalities are superior against tumors beyond the reach of older equipment. He believes that many of the inoperable lung cancers can be given good palliation with radiation therapy.

On the question, "should the patient be told?" -- two speakers cited patients who committed suicide when told they had cancer. Miller (U. of Mich.) stated: In most cases, the terminal patient should be sent home for better care than the hospital can give; every physician treating cancer should have a list of agencies that can help the terminal patient and the family; give the terminal patient drugs when
(Continued after page 180)

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Address all correspondence to
WILLIAM H. STONER, M.D., *Editor*
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a glance . . .

**one-minute abstracts
of the current literature on
radiation in cancer . . .**

X Rays Are Valuable

Newspapers, magazines, radio and medical journals lately have been reporting the harmful effects of radiation. Although knowledge of the quantitative aspects of the hazard is still crude, there is no doubt that ionizing radiation even in small quantities can be harmful to tissues—X rays are bad for people. But still the medical profession knows that, when skillfully used in diagnosis and treatment, X rays are good for people. Radiation therapy is consistently successful in curing some cancers and highly effective in relieving suffering in many forms of cancer at present incurable. Radioactive isotopes, which emit radiations essentially similar to X rays, are also of established value in clinical oncology. The use of radiation must be tempered by a knowledge of its possible harmful effects. Nearly every aspect of the practice of medicine is subject to possible harm; the most innocuous medicines sometimes cause serious anaphylactoid reactions. Awareness of possible dangers is a product of the physician's training and experience. Knowledge of the hazards of radiation sometimes leads us to advise against the use of X rays. No one should be exposed to even a small dose of radiation without adequate indication. The use of X rays when not really

needed is to be abhorred as much as the indiscriminate use of drugs. The high cost of medical radiation is some deterrent to its overutilization. Much can be done to reduce the hazards of radiation by the use of proper cones and filters, of full dark adaptation before fluoroscopy and of modern equipment regularly tested for safety. Increased attention to proper technique permits us to decrease substantially the radiation exposure of our population while the actual utilization of radiation in medicine is increasing. Like other iatrogenic dangers radiation hazards must be dealt with by knowledge, experience, perspective and common sense. Every practical technique to minimize exposure must be used for our patients, our helpers and ourselves. Only then can we be certain that the value of radiation outweighs its potential harm, and that X rays are good for people.

Raventos, A.: X-rays are good for people. [Editorial.] Pennsylvania M. J. 61:378-379, March, 1958.

Radioisotopes in Clinical Medicine

A radioisotope can be applied in the fields of biology and medicine when it can be used with safety for the patient and medical personnel, when it is superior to existing procedures and when the applica-

tion is simple and inexpensive. Radioactive iodine (I^{131}) is employed diagnostically in studying thyroid function, thyroid nodules and blood volume (radioiodinated serum albumin); therapeutically in thyrotoxicosis, thyroid carcinoma metastases and intractable angina pectoris and congestive heart failure. Radioactive phosphorus (P^{32}) is used in diagnosis of eye tumors (melanomas) and in the treatment of polycythemia vera. Radioactive gold (Au^{198}) is of special value in the treatment of carcinomatous effusions into serous cavities. Radioactive chromium (Cr^{51}) in the form of sodium chromate is useful in tagging red blood cells for determining red cell volume and survival. Radioactive cobalt (Co^{60}) is now widely used in the form of the teletherapy unit, the cobalt bomb and in needles substituted for radium needles. It is also useful diagnostically in the Schilling test for pernicious anemia by determining the presence or absence of the intrinsic factor in the stomach lining. When incorporated into vitamin B_{12} it is useful in the diagnosis of sprue.

Paulson, E. C., and Mosser, D. G.: Clinical applications of radioisotopes. Postgrad. Med. 23:493-498, May, 1958.

Electrolyte Disturbances with Radiation Therapy

Electrolyte imbalances occurring in patients undergoing radiation therapy comprise two major types: (1) those imbalances that result from the side effects of treatment—hypochloremic alkalosis from vomiting, potassium depletion alkalosis from inanition and hyperchloremic acidosis from diarrhea, and (2) those imbalances that are frequently associated with the types of malignant neoplasms treated with radiation—diabetic acidosis, adrenal insufficiency, renal shutdown and hepatic coma. The first problem in establishing an electrolyte diagnosis is to determine whether the condition is an acidosis or alkalosis, each being defined in terms of the alteration of the plasma pH. Normal extracellular pH is maintained at $7.40 \pm$

0.02 at 37° C. by renal and pulmonary means and by chemical buffer systems in the plasma, of which the bicarbonate is the most important. The plasma CO_2 reflects the pH and is the most readily obtainable measure of acid-base imbalance. Diabetic acidosis ranging from subclinical to frank diabetes occurs in about 35 per cent of all cancer patients, and in those with endometrial carcinoma the incidence is between 60 and 70 per cent. The alterations in carbohydrate metabolism in the cancer patient are frequently minimal and are controlled by diet alone. Ketosis frequently occurs during radiation therapy and, if not controlled, severe acidosis may result requiring treatment with bicarbonate and fructose, or with bicarbonate and glucose and insulin. Renal shutdown is one of the most frequent complications of advanced carcinoma of the cervix and other pelvic cancers. The two most significant chemical findings are an elevated potassium and an acidosis which is reflected in the decreased pH and CO_2 . Therapeutically, a protein-free, low phosphorus diet is prescribed and amphotril is given to bind phosphorus secreted by the gastrointestinal tract. The caloric content of the diet should be high to prevent breakdown of protein and the subsequent release of potassium and phosphorus. Fluids should be limited to 800 cc. per day plus the equivalent of the urinary output. Proper understanding of these syndromes and their management is important in patients receiving radiation therapy, for often the original plan of radiation therapy can be completed when in the past it had to be interrupted or abandoned.

Bane, H. N.; Glicksman, A. S., and Nickson, J. J.: Common electrolyte disturbances in the radiation therapy patient. Am. J. Roentgenol. 79:465-471, March, 1958.

Choice of Surgery or Radiation

Radiotherapy is now established as a therapeutic agent of immense value. There should be no prejudice or partisanship in the treatment of cancer—particularly car-

cinoma of the cervix, where it is of vital importance to the patient not to fall into the hands of either a surgical or radiation enthusiast, since each will use the method he knows best and this may not always be to the patient's best interest. Kottmeier has shown convincingly that with comparable clinical material radiotherapy gives results equal to those claimed by the surgeons. Radiotherapy is not only undoubtedly the correct treatment in inoperable cases but also usually the preferable treatment in operable cases. The authors report that their opinion based on experience since 1944 is that the results in stage I cases submitted to radiation treatment (60.4 per cent) compare favorably with those obtained when the Wertheim operation was performed (65.1 per cent). In these cases the authors customarily recommend radiotherapy with few exceptions. To be able with confidence to offer a patient the opportunity to avoid a major mutilating operation is regarded by the authors as a gesture in the best tradition of medicine and is a happy reward for their labors over the past years.

Blakley, J. B.; Lederman, M., and Simmons, C. A.: *Surgery or radium for cancer?* [Letters to the Editor.] *Lancet* 1:159-160, Jan. 18, 1958.

posure. The radiologist must be acquainted with the facts and persuade the patient of the much greater importance of obtaining necessary diagnostic data. The answer to the question "Are diagnostic X-ray examinations dangerous?" is "No" BUT in giving this answer the radiologist must be prepared to take all precautionary measures to protect the patient against excessive and unnecessary exposure. He must be prepared to reassure the apprehensive public. Among the safety measures are: the use of added filtration, cones and diaphragms; the use of higher kilovoltages; restricted fluoroscopy; short examinations of children; shielding the male gonads; restriction of examinations during pregnancy; abandonment of mass X-ray surveys; use of the fastest available films and fluorescent screens; good technique. Increasing use of X rays in medicine will not cause greater radiation dose to the population than is currently being received if the above measures are followed. Roentgen diagnosis entails only a minute hazard—a risk so small as to be negligible in comparison with the benefits derived.

Stapleton, J. G.: *Are diagnostic X-ray examinations dangerous?* *Canad. M. A. J.* 79:89-96, July 15, 1958.

Diagnostic X Ray

The whole subject of the biological effects of radiation is one in which knowledge is still somewhat limited. Dogmatic statements regarding dangers of diagnostic X ray may be based upon assumptions requiring revision in the light of future experience. The radiologist must admit that there is some room for improvement in practices regarding X-ray protection. Radiologists, X-ray technicians and the few workers with radioisotopes require special protective devices and practices. It has been shown by animal experiments and by human statistics that undue exposure to radiation shortens life. It is still better established that radiation is a biologic factor in leukemia. Numerous popular books and articles have alarmed the general public and many patients object even to the slightest diagnostic X-ray ex-

The Practitioner and Radiology

There is too great a reliance on X rays to the exclusion of accurate history taking and clinical examination—the use of X rays as a "penny-in-the-slot machine" method of diagnosis. This unjustifiable dependence on diagnostic radiology exists not only when positive changes are demonstrable but also in the absence of abnormal X-ray findings. A negative picture may mean that the lesion, for example, bronchial carcinoma, is too small to be detected or is masked by other structures. And occasionally, as in some early cases of cancer of the gastric fundus, it may be masked by the contrast medium. Every practitioner must today familiarize himself with the contribution of radiology to medicine; and every radiologist must keep abreast of the advancing frontiers of medicine, if he is to interpret his findings accurately. Radiology has not supplanted clinical

cal methods in medicine but is a unique tool in its service.

Cohen, M.: The physician's debt to radiology. Brit. J. Radiol. 31:170-173, April, 1958.

Co⁶⁰ in Cancer of Esophagus

The author believes that a re-evaluation of irradiation therapy for carcinoma of the esophagus must be made in view of the new rotational technique with cobalt-60. For the majority of patients with carcinoma of the esophagus treatment is purely palliative. Too many surgeons dismiss irradiation completely in spite of the much poorer results of surgical therapy. Six patients with histologically confirmed diagnosis of carcinoma of the thoracic esophagus were given a course of rotational cobalt therapy at Albert Einstein Medical Center (Philadelphia). The first patient died suddenly at home, probably of a cardiovascular accident. Five are living, one to five months, and are eating solid food. All were relieved of dysphagia on completion of treatment. Cobalt-60 teletherapy permits dosages beyond those possible from conventional deep X-ray therapy. Few systemic reactions are encountered, and, since there is less back scatter, the skin reactions are negligible. Reported operative mortality in carcinoma of the esophagus varies from 10 to 61 per cent. This newer application of radioactive cobalt is far superior to the several operative procedures, curative or palliative—esophageal dilatation, gastrostomy and intra- and antethoracic esophagejunostomy.

Sklaroff, D. M.: Rotational cobalt therapy palliation in carcinoma of the esophagus. J. Albert Einstein M. Center 6:54-57, March, 1958.

Radioisotopes in Cancer

The availability of radioactive isotopes has opened a broad new field in medicine, and particularly in the therapy of cancer of various organs. Cobalt-60 teletherapy—"the poor man's supervoltage"—has less skin reaction and greater penetration than conventional 200-250 kilovolt therapy. Cesium-137 is a practical source of supervoltage. It is a waste product of all atomic

piles and should be very economical. Strontium-90 is especially useful for lesions of the eye—lymphosarcoma and epithelioma. It emits no gamma ray and has poor penetration, sparing the radiation-sensitive lens. Tantalum-182 is flexible and can be molded to fit curved surfaces as in the bladder and about the eye. Radium and cobalt needles are rigid. Gold-198 is widely used in effusions due to malignant lesions and in carcinoma of the prostate and of the cervix. In effusions nitrogen mustard is less expensive and appears to be just as effective. Yttrium-90, also, is used like gold-198 in effusions. Iodine-131 is effective in therapy of less than 15 per cent of cases of thyroid carcinoma, mostly of the alveolar cell type. Phosphorus-32 is the drug of choice in polycythemia vera. It is also of value in chronic leukemia, and, when combined with testosterone, in bone metastases from breast cancer. It is not of great use in lymphosarcoma, plasma cell myeloma or Ewing's sarcoma.

Barnhard, H. J.: Artificial radioactive isotopes in cancer therapy. J. Arkansas M. Soc. 54:522-528, May, 1958.

Radiation and Public Health

The public health profession shares the responsibility for keeping the amount of radiation in the environment at a minimum, so as to reduce the threat to the health and life of the population. In New York State a Technical Advisory Committee composed of representatives of the medical and dental societies, the Atomic Energy Commission, the Public Health Service and independent radiation experts has set up a program for this purpose. Deliberations of the Committee developed the need for education, inspection, enforcement and research. The major objectives of a radiological health program are to prevent, reduce, or if possible, eliminate unnecessary exposure to ionizing radiation in the environment where people live, work and play. Such a program should determine the extent and character of the radiation problem; should reduce exposure to radiation by supervising installa-

tions and providing assistance to local health units in performing this supervision; and should obtain new information and develop methods of control by research and evaluation studies. The many critical questions raised concerning the use of X rays by physicians, dentists and other licensed practitioners should be answered by these representatives of public health. Mass chest X-ray surveys have been criticized and their benefits need to be currently re-evaluated in terms of the hazards involved. The dentist frequently takes several intra-oral films to make mouth examinations adequate. He has the same responsibility as the physician for having his equipment calibrated and for avoiding unnecessary exposure of himself and his patients. Medical and dental applications of radiation account for the largest part of the exposure, including fall-out, to which the human race is now being subjected. The New York Public Health Council adopted a regulation, effective July 1, 1958, prohibiting the application of radiation to human beings by anyone not licensed or authorized to practice medicine, dentistry, podiatry or osteopathy under the New York Education Law, except those under the immediate supervision of a licensed practitioner. Manufacturers can be prohibited from selling equipment to unlicensed persons. The regulations require registration of sources of radiation and reporting of changes in installations and of new installations. Rigid observance of prescribed rules on the use of radiation and on the use, storage, transportation and disposal of all radioactive materials is the only precise way of guarding against the hazards of excess radiation.

Hilleboe, H. E., and Rihm, A., Jr.: Program planning for radiological health. *Am. J. Pub. Health* 48: 965-970, Aug., 1958.

Toward Radiation Safety

Applications of machines producing radiation are not limited to the practice of medicine. They are used in industry, agriculture, food processing, dentistry and many other fields. Recently, the public

press has frequently referred extravagantly to the dangers of excessive radiation exposure and all radiologists have been embarrassed by patients with a little knowledge of the dangers of diagnostic X ray. The Surgeon General of the United States Public Health Service has formed a National Advisory Committee on Radiation including men in a broad range of scientific and ancillary disciplines, including radiology, radiobiology and radiation physics. This Committee will evaluate problems related to radiation and its hazards which affect the health of the operator and the patient. It is anticipated that this will result in a national program of radiation control and legislation. It is already apparent that there is great need for further development of fundamental and applied research in this field. The effects of radiation on biologic systems must be further studied. Scientific and medical schools need further facilities for radiologic education so that the supply of well trained specialists will be adequate. The author suggests that such a program be developed with entire scientific freedom with only such regulation as the public health demands.

Morgan, R. H.: Progress toward a comprehensive program in radiation safety. [Editorial.] *Am. J. Roentgenol.* 79:349-351, Feb., 1958.

Radiation in Pregnancy

The possible harm of irradiation to the pregnant patient should be known to the physician and weighed against the medical need. Physicians should take every precaution against radiation danger to self, staff and patients. Some idea of dosage may be had from the sum of all sources of natural radiation to which man has always been exposed—cosmic radiation, radioactive substances in the earth (uranium, radium, radon, etc.), radioelements in the body (K^{40})—a total of about 150 mr per year, or about 4 r total up to the age of 30. To this natural, background radiation has now been added the contamination from atomic industry, uses of radioelements, fall-out from nuclear explosions, occupational exposure (physi-

cians, nurses, dentists, workers in atomic industry, etc.), radium dial watches and instruments, and medical use of X rays, radium and isotopes. Of all these added hazards, the most significant by far is the diagnostic use of X rays. In the United States and Sweden, with the more excessive use of medical facilities the average exposure of the population has been estimated at from 10 to 100 per cent of the natural background. Exposure from fallout is less than 5 per cent of the natural dose. Excessive exposure may cause genetic harm to the race, or somatic harm to the individual—erythema, depilation, injury to fetus (abortion, abnormalities) and leukemia. Permissible dose up to age 30 is a total of 14 r. Average doses delivered to the maternal ovary by diagnostic procedures are: pelvimetry 1 to 4 r, urogram 1 to 2 r, barium enema or upper gastrointestinal tract 2 to 3 r, lumbar spine 1 to 8 r, chest (small cone) 0.07 mr. Single examinations may be of no significance, but repeated could become more serious. To minimize the dosages the exposure during the examination should be reduced by using smaller cones, higher kilovoltage, more filtration and faster screens and film. And fluoroscopy—a source of high dosage—should be avoided when possible. Especially in examinations of the pregnant woman should the number of films be kept at a minimum. The inlet view (Thoms) can be omitted in many cases. "Routine" pelvimetries are not indicated. Radiation required for diagnosis and treatment should be used, but its potentiality for harm must be weighed against the certain benefit to the individual.

Serber, W.: Indications and hazards of radiological procedures in pregnancy. J. Albert Einstein M. Center 6:69-72, March, 1958.

Hazards of Small Doses of Radiation

Many contradictory statements have been made concerning the possible hazards of small doses of radiation—the dosage incurred in most types of diagnostic examination. Available evidence suggests that there is no threshold of radiation for its genetic effects—the yield of mutations

is proportional to the dose and independent of fractionation and protraction. Clinical evidence shows an increase in leukemia as a possible result of radiation exposure of radiologists and radiation workers, survivors of atomic bombing, patients treated by radiation for ankylosing spondylitis, etc. and children whose mothers had pelvic and abdominal diagnostic X-ray examinations during pregnancy. The majority of human data on other tumors induced by radiation can be grouped as follows: (a) Tumors arising in various tissues following radiotherapeutic procedures, mainly tumors of skin and bone in adults, and cases of thyroid carcinoma in children. (b) Skin tumors in radiation workers, particularly early radiologists. (c) Bone tumors in radium miners. (d) Lung tumors in uranium miners. The present low incidence of leukemia in children would be about doubled if every pregnant mother had an abdominal diagnostic radiograph. Factors other than radiation must be excluded before acceptance of the reports showing abdominal radiation of the mother to be responsible for increase in incidence of leukemia in the child.

Lamerton, L. F.: An examination of the clinical and experimental data relating to the possible hazard to the individual of small doses of radiation. [The presidential address.] Brit. J. Radiol. 31:229-239, May, 1958.

Radiation—Respected not Feared

Diagnostic roentgenology is essential to the best practice of medicine and has contributed effectively to the health and welfare of our society. The hazards of radiation should be better known by the approximately 32,000 physicians, in addition to the radiologists of this country, who have diagnostic X-ray equipment. A recent survey showed leukemia to be decreasing among radiologists and increasing among nonradiologist physicians, reflecting the relative use of safety precautions. Similarly the radiologist can best protect the patient. The average skin dose of an adult PA chest film is 0.06 r, and of a lateral film, 0.12 r. In contrast the skin dose resulting from the fluoroscopic

chest examination with the average physician's office fluoroscope is about 30 r. The fluoroscope should not be used for screening and survey purposes. Radiation reaching the testes from fluoroscopy of the chest is 100 times that from a single X-ray film of the chest. Routine, periodic fluoroscopic examinations of well babies by the pediatrician should be discouraged. Radiation exposure of the physician, his staff and his patients can be reduced by periodic inspection and calibration of X-ray equipment by a physicist, use of 2 mm. of aluminum to filter out unnecessary radiation, use of higher kilovoltage with lower milliamps per second, use of effective shutters to minimize the area of exposure, use of field-limiting cones, diaphragms, faster film, screens and developer and use of lead rubber gowns and gloves and longer dark-adaptation (20 minutes) in fluoroscopy.

Sklaroff, D. M.: Radiation should be respected—not feared. [Editorial.] J. Albert Einstein M. Center 6:81-82, March, 1938.

Life Expectancy of Radiologists

The National Research Council, in a report on biologic effects of atomic radiation, stated that among these effects is shortening of the life span. This is not only a result of specific tissue damage, but also a result of general factors lowering immunity or hastening aging processes. Similarly the Medical Research Council in Great Britain found evidence of longevity of animals exposed to radiation. A survey of causes of death of medical practitioners in the United States disclosed that the average age at death of radiologists was 60.5 years, while that for physicians not known to have contact with radiation was 65.7 years. With some degree of exposure—gastroenterologists, urologists, etc.—the average age of death was 63.7. This report has been negated by a study showing that the differences in the age at death can be explained by differences in the age distribution of radiologists and other American physicians. There are fewer radiologists more than 65 years of age and they would, therefore,

be expected to die at a younger average age. If the age-specific death rates for all physicians at different ages had applied to the population of radiologists, their average age at death would have been 58.9 years instead of the observed 60.5 years. Thus, a statistical fallacy is prevented from becoming a "recognized fact." However, although there is little evidence of a shorter life in radiologists, American radiologists die of leukemia more often than other physicians. There were 17 deaths of American radiologists attributed to leukemia between 1938 and 1952, with 3.4 expected. Clearly, all reasonable precautions must be taken to protect radiologists from ionizing radiations, and the evidence does not, at present, indicate any failure to take them.

Anon.: Life expectation of radiologists. [Editorial.] Brit. M. J. 1:1112-1113, May 10, 1938.

Urologic Radiation Hazards

Although most of the operator's body can be protected from radiation by a lead apron, the hands are unprotected during such manipulation as retrograde urographic examination. A 90 per cent reduction in scatter irradiation reaching the urologist at the foot of the table may be obtained by covering the patient's thighs, buttocks, and genitals with a lead apron suspended by hooks from the crossbar which supports the X-ray tube. At the level of the genitals, a hole one and one-half inches in diameter is cut in the apron. The hole is then covered with lead rubber, overlapping the hole like a trap door. Catheters, special syringes and even the cytoscopic sheath may be brought out through the hole in the apron and used by the operator while roentgenograms are being made. The apron is also useful to the gynecologist doing contrast studies of the uterus as well as for general portable films. The lead apron shield is an adjunct to, not a substitute for, X-ray apparatus which meets current standards or for use of proper cones, diaphragms and filters.

Emanuel, M., and O'Connor, F. J.: Practical device to reduce radiation hazard in urology. J. Urol. 78: 192-195, Aug., 1957.

Radiation-Induced Tumors of the Mucosa

The carcinogenic effect of irradiation has long been known but the number of tissues susceptible is not generally appreciated. Skin cancer as a result of X or gamma irradiation is the most frequent and best documented entity. Relatively few studies have been made of carcinomas arising from mucous membranes and all those reported have been of the squamous cell type occurring either in the hypopharynx and larynx, or adenocarcinomas of the uterine corpus. The epithelium of mucous membranes, like that of the skin, is capable of malignant tumor formation as a late result of irradiation. Mucosal carcinomas developed in nine patients three to twenty-five years after irradiation. Lesions included six squamous cell carcinomas and three adenocarcinomas. Late radiodermatitis was usually apparent in the skin utilized for the external port and the tissues between the skin and affected mucosa were often fibrotic. The lesions appeared to be multicentric in origin and treatment was generally ineffective.

Slaughter, D. P., and Southwick, H. W.: Mucosal carcinomas as a result of irradiation. A.M.A. Arch. Surg. 74:420-429, March, 1957.

Chemical Radiation Damage

The ready availability of artificial radioisotopes over the past decade has increased the use of ionizing radiations as diagnostic and therapeutic agents. The present and potential exposure of human beings to radiation injury has increased still further with the introduction of atomic nuclear reactions as a source of energy in warfare and in industry. These circumstances have markedly increased efforts to uncover the mechanisms of the biologic action of ionizing radiations. Alpha, beta, gamma and roentgen radiations and neutrons produce similar biologic effects. Therefore, these effects can be studied by the use of the most convenient form of ionizing radiation X rays. Among the chemical tissue changes pro-

duced by ionizing radiations are those that can be expected to result from the action of products of irradiation of water. Reduced diphosphopyridine nucleotide, cytochrome C and sulfhydryl groups are oxidized, some enzymes are inactivated, and the properties of simple proteins and of nucleic acids are altered. Of special importance is the marked reduction of turnover of desoxyribonucleic acid in tumors and liver by radiation doses not greatly different from those producing obvious biologic effects. No single effect can be expected to be the foundation of all forms of radiation injury. Actual end results of radiation overexposure will vary not only because of the complex physical and chemical factors of energy absorption but also with the subtle organization and composition of the cells. One of the prominent features of radiation sickness is the attendant upset of salt and water metabolism consequent in part on vomiting, diarrhea and diuresis. Although the heart is not frequently thought to be radiosensitive, fluid and electrolyte disturbances following whole body irradiation of rats gave definite alterations in cardiac composition and function leading to death. Marked changes in the organic composition and fluid balance of the heart, increase of venous pressure, a tendency toward pulmonary edema, electrocardiographic changes and altered mechanical activity of the heart, all result from an LD₅₀ dose of X rays. The central nervous system, too, is usually regarded to be highly radioresistant. Yet, there are significant fluctuations in water, sodium and chloride contents of the brain following irradiation. There are also alterations from the normal desoxyribonucleic acid content and significant depletions of both the high and low electrocardiographic frequencies 3 to 12 hours following irradiation. Radiation damage is basically a chemical lesion affecting the composition and function of all cells and this lesion is produced by radiation doses lower than those causing anatomic damage.

Armstrong, W. C.: The chemical basis of radiation damage. Postgrad. Med. 23:499-507, May, 1958.



Keeping up

Breast Cytology

Cytologic examinations were made of cyst aspirates obtained from 100 patients. In addition 2010 patients were examined for the presence of nipple discharge. Of this number breast secretion smears were obtained in 1066 (50.5 per cent). Approximately half of the 2010 patients were asymptomatic and the others presented for examination because of breast disease including spontaneous discharge from the nipple. Of the 917 asymptomatic patients, 171 yielded secretion to palpation or the breast pump. From 74 of these, secretion was obtained bilaterally. More premenopausal than postmenopausal women yielded positive secretions. The peak was between ages 20 and 39 and in the fourth week of a regular menstrual cycle. Secretion smears from clinically normal breasts are sparsely cellular. In inflammations and infections the breast secretions have diagnostic characteristics. Malignant cells in breast secretion and cyst aspirate smears have characteristic nuclear abnormalities and other cytological criteria of cancer. Among 438 women without symptoms of breast diseases one was found by smear cytology to have unsuspected carcinoma in situ of the breast. Four cases of early, preclinical cancer of the breast were detected. Spontaneous nipple discharge should always be examined cytologically. Negative reports cannot be relied upon to rule out cancer, but positive reports are as reliable here as in any other cytological application.

Papanicolaou, G. N.; Holmquist, D. G.; Bader, G. M., and Falk, E. A.: Exfoliative cytology of the human mammary gland and its value in the diagnosis of cancer and other diseases of the breast. *Cancer* 11:377-409, March-April, 1958.

Causes of Disease

Probably no disease is any longer regarded as the result of a single agent but rather of a plurality of integrated conditions. These many factors are systematized by the author into (1) agents of disease—physical, chemical and biological, (2) host factors—inherent and acquired and (3) environment—physical, biological and social. The specific agents of disease are only rarely both necessary and sufficient causes. Diseases—infections (tuberculosis, poliomyelitis), diabetes, arthritis, psychoses, cancer—occur or are the result of a number of interacting factors of varying intensity and duration. Even though one may be able to demonstrate that a number of various factors influence the manifestation of cancer, none among them is regarded as the primary cause essentially deciding the nature of the disease. The symptoms are the result of the interplay of factors constituting the predisposing "milieu"—conditional, environmental and precipitating—each of which is in itself nonspecific. Precisely because of this aspect of both a multiple and nonspecific etiological concept, it is expedient for medical research to attempt to isolate and group fundamentally each of the various causal elements. Only in this way will it be possible to evaluate the importance of their duration, their relative weight and their interaction in the etiological causality pattern. Such systematic consideration of known etiological factors must inevitably clarify approaches for research into as yet unknown factors and yield valuable information concerning cancer.

Fog, M.: The causes of disease. *Danish M. Bull.* 5:41-47, Feb., 1958.

with Cancer



Uterine Cytology

Exfoliative cytology provides a simple and reliable method for the early detection of uterine cancer. Just as the periodic health examination is incomplete without a thorough vaginal examination, so is the pelvic examination incomplete without visualization of the cervix and a vaginal or cervical cell examination. The physician should examine the cervix for erosion, wart, ulceration, polyp, cyst, leukoplakia, consistency, movability, nodularity, and irregularity. Ulcerative and fungating lesions should be confirmed by biopsy. Vaginal and cervical smears should be taken and sent to approved laboratories for competent interpretation. The pathologist generally provides the directions for sampling. Vaginal pool aspiration is the simplest and most commonly used method, or material may be scraped off the cervix with a spatula, tongue blade or cotton applicator. The tampon method of self sampling may eventually prove to be the most satisfactory. The positive smears discovered in asymptomatic patients make the laborious screening of all patients well worthwhile. Cytology is primarily a prediagnostic method, revealing cases where biopsy is imperative. Therapeutic measures should be applied only after the positive smear has been confirmed by biopsy. And negative smears may infrequently occur in the presence of carcinoma. The practicing physician is the indispensable element around which the whole program of early cervical cancer detection by the cytological procedure must be built.

Nelson, H. M.: Exfoliative cytology in the detection of uterine cancer. Bull. Am. Coll. Surgeons 42:473-477; 506, Nov.-Dec., 1957.

The Cancer Patient

Should the patient be told he has cancer? Many variables influence the decision—the severity and prognosis of the cancer case as well as the personality and background of the patient. The competent care and individual consideration with which the approach is employed in addition to the initial decision determine success. Certain types of cancer cases lend themselves more simply and successfully than others to the so-called completely truthful attitude of physician: the less incapacitating and easily curable cancers not often associated with misery and death such as in-situ and borderline cancers that arise in precancerous lesions of the skin and basal cell cancer of the skin. Localized and well encapsulated cancers that do not spread or metastasize for many years fit this category. Mixed tumors, some encapsulated adenocarcinomas arising in carcinomas and certain sarcomas (fibrosarcomas) that are histologically malignant but clinically benign are also included. Since these cases have a relatively good prognosis, an optimistic point of view may be transferred to the patient even when he is confronted with the true nature of his disease. Usually a proper approach to suitable members of the family will greatly relieve the burdens of business and family affairs and other obligations of the patient. Proper ambulatory or home symptomatic care with the cooperation of the family—the attempt to maintain an active and useful existence for the patient—will make the best of the worst of cancer.

Sage, H. H.: The approach to the cancer patient and his family. New York J. Med. 58:1928-1930, June 1, 1958.

Radiation Is a Carcinogenic Agent

C. Lenore Simpson, D.M.

The first cancer attributed to roentgen rays was reported only six years after their discovery.²² In the early years the tumors were occupational because of lack of knowledge about the dangers of this new and fascinating agent. Measures were soon taken to prevent the more obvious types of over-exposure but even now over-exposure occurs in unexpected places. Reports of occupational tumors were followed in a few years by reports of tumors occurring after therapeutic measures and these now predominate in the literature. During the half century that radiation cancer has been known the amount of exposure recognized as harmful has steadily been lowered until there is argument as to whether a threshold exists below which tumors are not induced. At the moment, a relentless search is being made for evidence on this point in both man and the experimental animal. In the meantime, anyone in the position to expose either himself or others to radiation in any form should be aware of the evidence and of the possible degree of risk as it is at present known.

Many different types of cancer are known to follow radiation, and tumors are apparently induced more readily in some sites than others. Tumors may be superficial or involve deep organs, and they may follow roentgen-ray exposure or exposure to radioactive isotopes. The latter is frequently a chronic exposure to small amounts of radiation due to retention within the body for a long period.

Most of the skin cancers which follow radiation are squamous cell carcinomas. In general, they are preceded for several years by a chronic dermatitis characterized by atrophy and sometimes ulceration of the skin. These cancers are often multiple and the prognosis is poorer than of that of the usual skin cancer.²² Although in general, repeated exposures pre-

cede the disease, it has been reported after a single exposure.¹⁸ The latent period ranges from four to 42 years.²²

There is no clear evidence as to whether the incidence of skin cancer is increased among the many people who have received relatively small amounts of radiation for nonmalignant skin conditions. Many cases have been reported following treatment of such conditions as acne, but these patients had usually received what would now be considered excessive amounts of radiation. The reported surveys which claim no danger from "properly applied" radiation in the hands of dermatologists are inadequate because of the very low percentage of patients followed, the short follow-up period in relation to the long latent period of the disease and failure to define exactly the selection of treated and control cases.^{1, 20}

Cancers of mucous membranes have been reported fairly frequently following radiation but tumors are common in many of these sites apart from radiation. Goolden has recently reviewed the reports of cancer of the pharynx following therapeutic radiation. Some of these cases showed little or no evidence of changes in the overlying skin. One group of cases followed radiation for thyrotoxicosis. Goolden calculated that too few patients in the area had received radiation for thyrotoxicosis for this to be a chance occurrence. Therefore, he felt justified in attributing a large proportion of the cases to the preceding radiation.

Although Goolden's study is by no means ideal, it gives the best evidence available at the moment. The latent period of the cases he reports lies between 10 and 35 years with a mean of 25 years. We can examine some of the other reported cases against this background. Slaughter reported two adenocarcinomas of the colon occurring three and four years after treatment. It is rare to find carcinomas of the gastrointestinal tract attributed to radi-

Department of Pathology, Roswell Park Memorial Institute, Buffalo, N. Y.

ation. The relationship of these lesions of the colon can be questioned on the basis of the very short latent periods alone. Both X rays and radium have frequently been used to treat excessive uterine bleeding, and most pelvic organs are common sites for malignant tumors. A few postradiation surveys have been made of patients who received such treatment. The most extensive of these²⁰ was conducted after a minimum period of 16 years following radiation treatment. The authors found a considerable increase in tumors of the reproductive organs and also of the rectum and bladder. Unfortunately they analyzed only 721 replies from over 1600 women originally treated. As their position was such that they were more likely to find patients who developed cancer the results must be considered biased. Carefully controlled epidemiological studies will be needed to demonstrate an increase in this type of cancer following radiation.

The possibility of cancer of the thyroid following radiation has become very important in the last few years because of the introduction of radioactive iodine. Although external radiation had been widely used in the treatment of hyperthyroidism few cases of thyroid cancer had been seen following its use. Reports of cancer developing in a normal gland included in a radiation field were practically unknown until 1950.⁶ A few years later, in a survey of over 2000 children who had received radiation to the thymus, it was found that 20 had had thyroid operations by the age of 20. Half of these were for carcinomas, the others for nonmalignant nodular lesions.^{24, 25} As only one sibling had had an operation on the thyroid, this was obviously not due to environmental factors. The incidence of thyroid tumors seemed to be highest among the children who received the most radiation, which strongly suggests that these tumors were a result of the treatment. About the same time, Clark reported that all thirteen of the children he had seen with cancer of the thyroid had had previous radiation treatment about this area. A minority of children had received radiation to the thymus, the others received treatment to

cervical lymph nodes or nasopharyngeal lymphoid tissue. These reports have been followed by others with similar findings,^{7, 23} and radiation may be playing a part in thyroid cancer in the older age groups as well.^{2, 19, 24}

The remarkable fact about the thyroid cancer cases is that the majority show no radiation changes in the overlying skin. In most of the reported cases, the skin dose has been between 400 and 700 r with the thyroid probably receiving less than this. Previously, cancer in man was rarely reported after less than 1000 r of radiation.¹¹ In addition, these cancers are appearing after a relatively short latent period.

A considerable number of sarcomas, particularly of bone, have been reported following external irradiation. While many of these occurred in previously diseased bone, many have arisen in previously normal bone included in a radiation field. The majority of the tumors followed large, frequently excessive, amounts of radiation as indicated by associated growth disturbances and radiation dermatitis or osteitis, although occasional tumors have been reported with as little as 1000 r original tumor dose.⁵ The latent period ranged from four to over 20 years. As among the thyroid tumors, there is evidence that benign tumors may occur at lower levels of radiation in susceptible persons.^{5, 19, 24} Such a tumor has even been seen following fluoroscopy during removal of a foreign body.¹⁵

Tumors of the central nervous system have rarely been attributed to radiation in man but Mermann and Dargeon found that two of four deaths among their cases of Hand-Schüller-Christian disease were due to brain tumors. Both of these children had received radiation to the skull. No details of treatment were given. Strauss and Kligman showed that in adequate routine therapy for ringworm, skin doses vary from 340 to 660 r at different points on the scalp and some 25 per cent of this amount penetrated the skull. No brain tumors have been reported following therapy for ringworm but the only follow-up surveys of groups of children treated for

ringworm are inadequate in number and length of follow-up.^{25, 30} Extension of such surveys should probably be undertaken.

Some of the data on radiation-induced cancer are inseparable from the data on leukemia induction. For instance, the incidence of leukemia as well as of thyroid tumors was high among the children surveyed following thymic radiation.²⁴ Stewart found that diagnostic X-ray examinations of the pelvis during pregnancy had been twice as frequent among the mothers of children who subsequently developed leukemia or other malignant tumors. Neither finding is significant in itself, but both suggest the possibility that very small amounts of radiation and partial body irradiation may be leukemogenic in man. An increased incidence of leukemia has been shown following the atomic explosions in Japan¹⁴ and radiation for ankylosing spondylitis.⁴ There is evidence that the increase is higher among the individuals receiving the larger amounts of radiation. In both cases, the amount of radiation was much greater than that received by the infants mentioned above. Court-Brown and Doll conclude from their data that very small amounts of radiation may be leukemogenic and postulate that there may be no threshold level for leukemia induction. Certainly, there is evidence from the number of radiologists who die of leukemia that repeated, very small exposures to radiation may be leukemogenic.²¹

The previous discussion has been largely restricted to roentgen rays. Radioactive substances present a somewhat different problem owing to the possibility that they may be retained in the body for long periods. The emission of various types of radiation results in various clinical pictures determined by the place of storage, the penetration of the radiation, the half-life of the isotope and other factors.⁹

Exposure to radioactive substances may be occupational or medical. Seventy-five per cent of the Schneeberg miners are said to have died of cancer of the lung in recent years.¹¹ This is by far the highest cancer rate claimed to have followed ex-

posure to radiation in man. So far, similar reports have not come from other areas but it must be remembered that uranium mining on a large scale is relatively recent. A small number of carcinomas of the nasal sinuses and nasopharynx have also followed exposure to radioactive materials. Only eight bone sarcomas are known to have developed among the original 800 radium dial painters¹¹ although the mortality from other complications was much higher. However, other bone sarcomas have occurred among people who absorbed radium, sometimes from medicinal sources.¹⁶ Although the severity of radiation osteitis tends to increase with the radium load, no clear relation between this and tumor incidence can be shown. This is probably due to contamination of the original radium sources with substances such as mesothorium which are differently distributed in the body and may be more active in producing sarcomas.

The introduction of thorotrast as a diagnostic tool also resulted in the production of tumors. As so often happens, a ten-year follow-up³¹ revealed no evidence of ill effects, yet a few years later several tumors were reported.

Leukemia is the only complication reported in any numbers after the current use of radioactive isotopes in medicine. Several cases have been reported following the use of iodine-131 in carcinoma of the thyroid.⁴ It is still too early to assess the likelihood of thyroid cancer after the use of this isotope. The few cases so far reported are not sufficiently above the expected number to be significant.⁸

Conclusion

The evidence presented has shown that many types of cancer are known to follow radiation. It will be noticeable, however, that information is lacking as to the frequency of tumors following different types and degrees of exposure in man. All the evidence suggests that a relatively small number of exposed individuals develop cancer, although this proportion

tends to rise with increased intensity of the original radiation. The latent periods are long, and it is probable that many more individuals would develop cancer if they did not previously succumb to some other disease. The use of radiation in its many forms is increasing rapidly both in industry and medical practice. At the present time, medicine is contributing a greater addition to the background radiation than industry or fall-out and it is likely to do so for a considerable time to come. All physicians and dentists should consider, before exposing a patient even to diagnostic roentgen rays, whether the

information to be obtained is necessary. Diagnostic techniques should expose the minimum consistent with their purpose and the fluoroscope should be avoided unless essential. This is a good principle, even though the risks of a single diagnostic exposure are infinitesimal, because of the known cumulative effects of radiation and the many possible reasons for its further use. Exposure of children, in particular, should be avoided as far as possible because of their long life expectancy and experimental evidence that immature animals may be more susceptible than adults.¹²

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Fig. 1



Fig. 2



Fig. 3

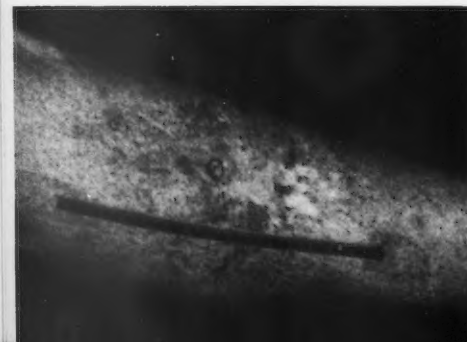


Fig. 4

LATE RADIATION

Figure 1. Age 65. In 1932 this 40-year-old woman was treated surgically and subsequently by irradiation for brain tumor resulting in permanent epilation four months later. Twenty-five years later, basal cell carcinoma of scalp developed in original field of radiation.

Figure 2. Age 36. Thirty years ago in Germany this 6-year-old girl was treated for tinea capitis with radium mold effecting permanent epilation. Twenty-seven years later, meningioma developed. After surgical excision scalp wounds failed to heal.

Figure 3. Age 38. In 1933 patient had X-ray treatment for acne and hirsutism. She has had numerous excisions and skin grafts since first basal cell carcinoma appeared in 1943. Basal cell carcinoma on bridge of nose with multiple telangiectasia present in 1957.

Most of the cases presented here were first reviewed in connection with the Program for Modification of Late Radiation Changes, Division of Clinical Investigation, Sloan-Kettering Institute for Cancer Research, and the Department of Radiation Therapy, Memorial Center for Cancer and Allied Diseases, New York, New York. Illustrations provided by James J. Nickson, M.D. and Arvin S. Glicksman, M.D.

Figure 5A, B and C. Courtesy of Norman L. Higinbotham, M.D., Bone Tumor Service. Figure 12. Courtesy of Richard S. Benua, M.D. and Rulon W. Rawson, M.D., Division of Clinical Investigation.

Fig. 5A



ATION CHANGES

Figure 4. Age 46. Patient had psoriasis at 13 and was treated intermittently with X rays to the trunk and lower extremities over 19-year period. In 1943 and 1947 radiation-induced ulcers were excised but ulcer recurred. In 1950 histological examination of lesion was reported as squamous cell carcinoma.

Figure 5. Age 15. At the age of 1, patient had received intensive irradiation for large cystic hygroma of neck. A, Osteochondroma of head of left humerus only pathologic finding at 9 years of age. B, Five years later, advanced inoperable postradiation osteosarcoma of clavicle. C, Extensive radiation damage to skin—atrophy, necrosis and ulceration—with marked retardation of growth of clavicle, scapula and humerus.

Figure 6. Age 51. This 31-year-old woman was irradiated for tuberculosis of bone in 1937. Immediate radiation reaction developed. Squamous cell carcinoma in 1957 after three plastic repairs on right leg.

Figure 7. Age 60. A, Basal cell carcinoma of nose treated by radium mold in 1955. Radiation necrosis developed. B, Three years later ulceration in marginal area of original basal cell carcinoma. Ulceration healing.



Fig. 7B



Fig. 7A



Fig. 5B



Fig. 6



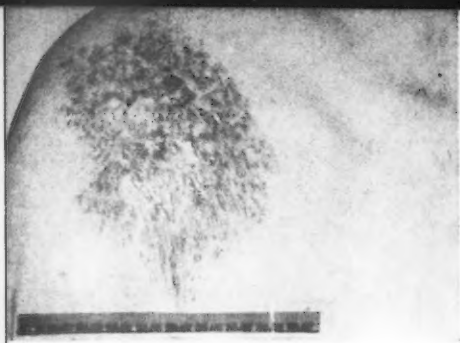


Fig. 8

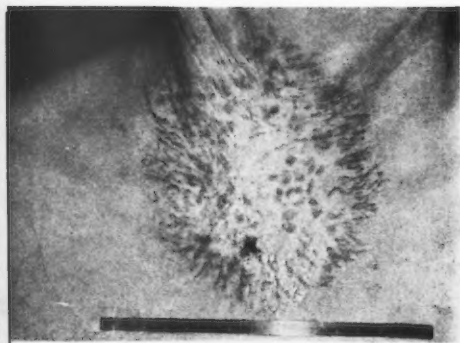


Fig. 9



Fig. 10



Fig. 11A

Figure 8. Age 61. This 52-year-old man received X-ray therapy for bursitis in 1949. Three months after treatment ended he complained of pain, tightness and burning of skin. Progressive skin changes first noted in 1951. Appearance in 1958.

Figure 9. Age 57. In 1929, this 29-year-old man was irradiated for a small cyst under skin of lower part of neck near rib-line twice a week for one year with open glass tube, apparently a Coolidge tube. Twenty-eight years later, typical postradiation changes—dryness, loss of hair, telangiectasia, hyperpigmentation and dry desquamation.

Figure 10. Age 51. In 1937, this 40-year-old veterinarian had a superficial fungus infection of both hands and feet treated by X ray intermittently until 1943 resulting in marked blistering and desquamation at that time. In 1946, ulcers on both feet necessitated pinch grafts that took on right foot only. In 1948, ulceration and superficial epidermoid carcinoma of right foot. Follow-up: Bilateral mid-leg amputation for radiation necrosis of bone.

Figure 11. Age 80. In 1900, this 22-year-old woman required diagnostic X-ray examination of knee. She was exposed for more than an hour. Prompt appearance of acute skin reaction necessitated skin graft in 1901. A, Appearance of knee burn in 1958. B, Roentgenographic appearance showing no pathologic change.

Figure 12. Age 22. A 13-year-old boy with a history of recurrent rheumatic

Fig. 11B



Fig.

disease, mitral stenosis and irradiation in infancy was seen at Memorial Center in 1947. Papillary and alveolar thyroid carcinoma metastatic to lungs and enlarged lymph node in neck present. In October, 1948 roentgenographic appearance of chest shows nodular carcinoma with metastases to both lung fields. From 1949 to 1953 tumor uptake was increased with thiouracil and I^{131} therapy with marked diminution of pulmonary metastases. Follow-up in October, 1956: Feeling well and working every day.

Figure 13. Age 86. In 1950, this 80-year-old radiologist had amputation of distal phalanx and small portion of middle phalanx of third left finger for radionecrosis with marked telangiectasis. Chronic radiation dermatitis for 47 years.

Figure 14. Age 56. Occupational exposure to formalin resulted in severe dermatitis in 1941 for which this 40-year-old undertaker had X-ray therapy. Amputation advised for squamous cell carcinoma.

Figure 15. Age 37. Patient received X-ray therapy for fungus infection 20 years ago resulting in typical thinning and atrophy of skin and loss of subcutaneous tissue around nails.

Figure 16. Age 60. Dentist with 20 years' occupational exposure to X ray showed progressive changes for last five years. Index and middle finger of both hands show typical fibrotic telangiectatic changes compatible with diagnosis of post-radiation changes.



Fig. 16



Fig. 15



Fig. 13



Fig. 14

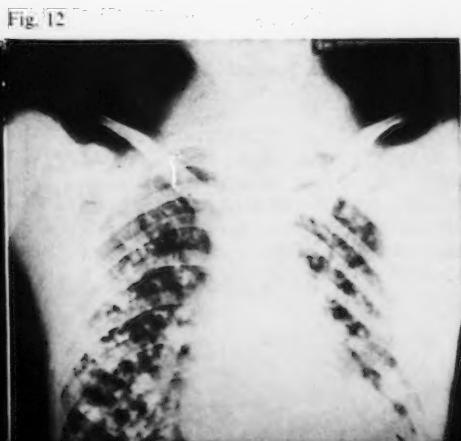


Fig. 12

Radiation in the Treatment of Cancer

Gilbert H. Fletcher, M.D.

The cancer literature is filled with claims that either surgical intervention or radiation is superior in the treatment of malignant tumors. Actually, the controversy is limited to approximately one fourth of the clinical material as, for instance, radiation therapy has no place in the gastrointestinal cancers which alone comprise approximately one third of all cancers. Too often data are based on selected series. The significance of these claims is further limited due to the great difference in quality of the clinical material of reporting institutions.

In addition to destruction of the tumor, either surgically or radiotherapeutically, various degrees of preservation of function or cosmetic aspects should be taken into consideration.

The respective places of radiation and surgical resection have changed in the last twenty-five years. A quarter of a century ago, radical surgical procedures were fraught with appreciable mortality and considerable morbidity and, therefore, had to be reserved for favorable cases. Nowadays, radical operations, with almost no operative risk, can be used for palliative therapy.

Until recently radiotherapy was not a formal discipline with indications and techniques. Radiotherapeutic techniques, aided by radiophysics and new tools (supervoltage, isotopes), have been integrated with clinical experience in a discipline which forms one of the specialties of medicine. These disciplines, surgery and radiotherapy, are too complex for any one person and require separate specialists.

Radiation therapy is indicated in a wide spectrum of situations. For instance:

Department of Radiology, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

I. For cure:

A. Alone, without any alternative, as for tumors of the nasopharynx; or as an alternative to resection, as for tumors of the tongue, vocal cords, uterine cervix, etc. In these groups, in addition to survival rates, preservation of function and ease of achieving results must be considered.

B. In combination with surgical procedures: There are groups of tumors in which either discipline yields unsatisfactory results alone, and significantly better only by planned sequential procedures.

II. For palliation: Palliation should not mean treatment of every patient with cancer on the general principle that some sort of treatment will necessarily prolong life or make it more comfortable. There must be a symptom to alleviate or a definite purpose to achieve.

A. Long range palliation: The local control of lymphomas and breast tumors no longer suitable for primary radical mastectomy can result in long symptom-free periods of life.

B. Short range palliation for the relief of a distressing symptom: This is well illustrated by reopening of the lumen of the esophagus, or regression of mediastinal nodes in the oat cell carcinomas of the lung.

C. Simple relief of pain.

Head and Neck Tumors

The management of head and neck tumors is brought to its maximum effectiveness for preservation of both life and function by a team of surgeon and therapist. The two methods of treatment are interwoven in the management of the primary and neck nodes separately or as a whole.

Radiation therapy almost systematically controls the primary and neck metastases of nasopharyngeal tumors. The fate of the patient is determined by distant metastases or intercurrent diseases.

Tumors of the oropharynx (tonsils, base of tongue, pharyngeal walls) and the palatine arch (anterior faucial pillars, retromolar trigone and soft palate) are best handled by radiation—alone, or followed by resection. Supervoltage is of advantage in this area.

The various sites of the oral cavity must be judged on their own merits and plan of treatment made by the surgeon-therapist team. The tumors of the anterior two-thirds of the tongue (see Table I), of the buccal mucosa and, to a lesser degree, of the floor of the mouth are controlled very effectively and with good preservation of

function by radiation therapy. The alveolar ridge tumors are not managed on a general policy, but on individual appraisal, depending upon extension and bone involvement.

The treatment of early squamous cell carcinomas of the vocal cords constitutes some of the most gratifying experience of the therapist. Cure rates are very high. The normal voice is preserved to a degree unmatched by partial laryngectomies (see Table II).

Paranasal sinuses and extrinsic larynx tumors require combined resection and radiation with sequences and techniques depending upon site and extensions.

Metastatic neck nodes from the keratinizing squamous cell carcinomas are best managed by neck dissection, but when the nodes are large or the tumors are anaplastic (oropharynx and extrinsic larynx) combined radiation and surgical procedures enhance the possibility of control of the disease.

Tumors of the Thorax

In this area therapeutic radicalism of any kind yields less than 5 per cent five-

TABLE I

55 SQUAMOUS CELL CARCINOMAS OF THE ANTERIOR TWO THIRDS OF THE TONGUE

4-Year Radiotherapeutic Results			
	Alive 25	Dead 30	
No Node	18	8	6 intercurrent disease
			1 no data
			1 failure to control a massive primary
Nodes*			
Unilateral †	7	8	
Bilateral †	0	14	

* Neck nodes treated by radical neck dissection.

† Metastatic nodes, unilateral or bilateral, at any time during the course of the disease. The control of the primary lesions has been systematic unless the disease was very extensive. In three instances, a limited recurrence after radiation has been successfully removed surgically. Age and metastases to the neck or at distance are responsible for failures.

TABLE II

51 SQUAMOUS CELL CARCINOMAS OF VOCAL CORDS

3 to 9 Years' Follow-up

Early*	28
Partial fixation or both cords involved	16
Completely fixed (coronary status preventing laryngectomy)	3
Unspecified involvement	4
Alive	39
Dead (all from intercurrent disease)	12

* Limited to one cord with no limitation of mobility.

Two recurrences were treated by laryngectomy. One patient died from intercurrent disease in the seventh year, and the other is alive, with no evidence of disease, four years later. The voice is entirely normal in more than two thirds of the patients and only mildly husky in others.



Fig. 1. Top, A case of inflammatory carcinoma treated by radiation alone. The patient is alive and symptom free at five years.

Figs. 2 and 3. Middle and Bottom, These two cases were managed by simple mastectomy followed by heavy irradiation to the chest wall and peripheral lymphatics. The patients are alive, with no evidence of disease nine years and six years later.

year survivors in an unselected series.

By comparing the results of radiotherapeutic and surgical series in cancer of the esophagus, almost all the survivors of the surgical series had lesions in the lower third, while the greatest number of survivors treated with radiation had disease in the upper third. This delineates the respective areas of the two methods.

In cancers of the lung, radiation must be used very conservatively. A patient with an inoperable cancer of the lung and only a few months of remaining life should not be treated just because he has cancer. Irradiation is most useful to produce regression of upper mediastinal nodes (usually oat cell tumors) in order to substitute a more merciful modality of death than the one associated with a superior vena cava syndrome. The so-called Pancoast's tumors can also be irradiated without too much discomfort, often with relief of pain and perhaps some increase in life span.

Tumors of the Breast

Irradiation of supraclavicular and internal mammary chain nodes after radical mastectomy is an accepted routine, but its value has not been demonstrated.

Radiation is most helpful in cases no longer suitable for primary radical mastectomy (Figs. 1, 2 and 3). The last twenty-five years have shown that resection can be not only futile, but positively harmful. Technical and clinical criteria, like those established by Haagensen, define the line for primary radical mastectomy.

Tumors of the Urinary Bladder

After disappointing results in the early days of radiation therapy, bladder tumors have been handled by various degrees of surgical radicalism. The results of the total cystectomies, with their functional and metabolic complications, have also been disappointing and there is a revival of interest in the use of irradiation for tumors which have invaded throughout

the bladder wall. Supervoltage therapy is much superior to conventional 250-kv. therapy.

Tumors of the Testes

The effectiveness of radiation to the periaortic node metastases in the seminomas is well established. There is some uncertainty concerning the usefulness of postoperative irradiation to the periaortic nodes in the embryonal carcinomas and the teratomas. Retroperitoneal lymphadenectomies and irradiation should complement each other.

Lymphomas

Radiation is the best treatment for Hodgkin's disease unless it is very generalized or there is extensive involvement of organs. The lymphosarcomas, either reticulum cell, small cell or giant follicular, show practically no response to chemotherapy and therefore are treated almost entirely by radiation no matter how widespread.

Cancers of the Uterine Cervix

Stage for stage and for the cases as a whole, there are no surgical results which have matched radiation results. Several radiotherapy centers of the world report 80 to 90 per cent cure rate in stage 1, 60 to 70 per cent in stage 2, 30 to 40 per cent in stage 3 (see Table III).

Cancer of the Vagina and Female Urethra

Radiation therapy is very effective in tumors of the vagina and the female urethra, and supervoltage has added greatly to this effectiveness. Unless very advanced, local control of these tumors is now the rule.

Ovarian Cancers

The surgical management of ovarian tumors leaves much to be desired, as tumor tissue is left behind most of the time.

Radiation plays a role which ranges from cure in some cases to relief of pain or of ascites in others.

Radioresistant Tumors

For the most part, irradiation has no place in the glioblastomas, the soft tissue sarcomas, melanomas or in the carcinomas of the gastrointestinal tract. In selected instances, some temporary benefits can be achieved with radiation.

Miscellaneous Tumors

There are a number of rare tumors which respond to radiation. However, space does not permit detailed coverage here.

New Radiotherapeutic Tools

There are two new tools which have come to the forefront: radioisotopes and supervoltage.

Radioactive isotopes have added little to the treatment of patients with cancer. The rare thyroid carcinomas taking iodine are less than one case in a thousand. Radioactive phosphorus has been almost supplanted by chemotherapy.

Gamma-ray emitters (cobalt-60, cesium-137, etc.) occasionally offer some extra flexibility for interstitial or intracavitary gamma-ray therapy.

Radioactive colloidal gold or chromium phosphate are useful in the palliation of malignant effusions.

Supervoltage roentgen therapy (million volt X-ray generators, teletherapy units, and the like) has the obvious advantages of skin-sparing effect, greater depth dose and better systemic tolerance. The cancers amenable to conventional methods (early carcinomas of the oral cavity, of the vocal cords, the stage 1 and early stage 2 carcinomas of the uterine cervix) do not benefit by supervoltage.

Where interstitial or intracavitary radium cannot be used (oropharynx, advanced urinary bladder tumors) or where it is inadequate (late cases of cervical carcinoma) supervoltage may increase con-

trols and survival time.

More effective and better tolerated combinations with surgical resection are also possible with supervoltage therapy.

Supervoltage therapy is likewise a better tolerated palliative agent for the mediastinal or abdominal radiosensitive tumors (lymphoma, testicular tumors, etc.).

Although it is very hard to prove the superiority of supervoltage therapy in terms of figures, it is being used more due to its advantages. It should not, however, be construed as a panacea. Radioresistant tumors, generalized cancers and post-radiation recurrences should not be irradi-

ated with supervoltage just because there is no skin reaction.

Despite advances in technology, therapists must essentially be observers of the natural history of cancers, with experienced clinical judgment. Cancer therapy has become very complex and the various disciplines have grown too much to be combined in one individual. In cancers of head and neck, breast, thorax, urinary bladder and genital tract only a surgeon-radiotherapist team can offer the best choice of treatment or the most effective combination of treatments based on objective facts, all extraneous factors having been set aside.

TABLE III
FIVE-YEAR SURVIVAL IN SQUAMOUS CELL CARCINOMA OF CERVIX PREVIOUSLY UNTREATED
(Excluding Carcinoma of Cervical Stump)

	ALL REGISTERED CASES			ALL TREATED CASES		
	Total No. Pts.	No. Pts. Alive	Survival Rate (Absolute)	Total No. Pts.	No. Pts. Alive	Survival Rate (Relative)
STAGE 1	64	57	89%	64	57	89%
STAGE 2	254	168	66%	252	168	67%
Early*	129	95	74%	129	95	74%
Late	125	73	58%	123	73	59%
STAGE 3	208	63	30%	180	63	35%
Early†	98	39	40%	93	39	42%
Late‡	110	24	22%	87	24	28%
STAGE 4	63	1	1%	19	1	5%
STAGE 1 and STAGE 2 Early	193	152	79%	193	152	79%

The incidence of stage-1 cases is 11 per cent of all cases registered. Thirteen per cent of the cases registered were considered too advanced for any treatment. All patients were traced. Patients dead from intercurrent disease are counted as failures.

*Technically suitable for radical hysterectomy.

†One pelvic wall involved or only lower third of vagina.

‡Frozen pelvis or near frozen pelvis.

Books of Current Interest

THE LOVE OF A PHYSICIAN—GEORGE E. PFAHLER, M.D., PIONEER RADIOLOGIST. By MURIEL B. PFAHLER. Philadelphia. Dorrance & Company, Inc. 1958. 274 pages. \$3.75.

The title of this unusually interesting biography might well have been "The Three Loves of a Physician"—radiology, photography and the author. Mrs. Pfahler has skillfully recorded her doctor's many contributions to the development of the science and art of radiology, his talent in photography and their travels to the leading radiological centers of the world. This biography of the doyen of American radiology constitutes a veritable history of the science from Roentgen's discovery to the leukemic martyrdom of Dr. Pfahler on his 83rd birthday anniversary. His scientific contributions are interestingly interspersed with personal anecdotes told in a fascinating manner by his sympathetic partner. The book will be of great interest to all radiologists, to all who knew Dr. Pfahler professionally and personally, to his many undergraduate and graduate students in all parts of the world, to everyone interested in photography and especially to their distaff contingents.

MEDICAL RADIATION BIOLOGY. By FRIEDRICH ELLINGER, M.D. Springfield, Ill. Charles C Thomas. 1957. 945 pages. \$20.00.

The Chief Radiation Biologist of the United States Naval Medical Research Institute reviews the literature of the entire subject of medical radiation biology. Three-unit numbering of the chapters and paragraphs, an alphabetical bibliography of 4600 entries all with paragraph references, numerous footnote cross references, and a detailed, 22-page Contents make an index unnecessary. The text is divided into four parts: fundamental radiation biology, biology of ionizing radiations, biology of ultraviolet radiation and photobiology. The book is an excellent, comprehensive, convenient and meticulously prepared and published guide to the literature through 1954.

1896—Vienna and Chicago

The noise of the war's alarm should not distract attention from the marvelous triumph of science which is reported from Vienna. It is announced that Prof. Routgen [sic] of the Wurzburg University has discovered a light which for the purpose of photography will penetrate wood, flesh, cloth, and most other organic substances. The professor has succeeded in photographing metal weights which were in a closed wooden case, also a man's hand which showed only the bones, the flesh being invisible.

Daily Chronicle [London], Jan. 6, 1896.

According to the records of E. H. Grubbe of Chicago, he began x-ray treatment of a cancer of the breast by Jan. 29, 1896 (twenty-three days after the announcement of the discovery in the newspapers), and the next day applied the rays to a case of lupus vulgaris. Grubbe was at that time a manufacturer of Crookes tubes, and the patients were referred to him by two physicians on the staff of the Hahnemann Medical College (Chicago), where his hands were being treated for a dermatitis evidently due to exposure to the rays. Roentgen therapy thus began almost exactly with the discovery of the rays and, so far as is known, was first practised in America.

Pfahler, G. E.: The development of roentgen therapy during fifty years. Radiology 45:503-521, Nov., 1945.

Autoradiography

Patrick J. Fitzgerald, M.D.

The atomic era was, in one sense, opened by an autoradiogram. For, after the French physicist Becquerel had unintentionally placed in a desk drawer a piece of uranium ore on top of a light-protected photographic emulsion, he noted after subsequent development of the photographic emulsion an image of the uranium rock present in the emulsion. Thus the physical juxtaposition of a radioactive ore and photographic emulsion with the added apposition of a trained and inquisitive mind opened the Pandora's box of natural radioactivity.

Relatively little use of the method was made in the early part of the twentieth century except for occasional utilization by such distinguished continental scien-

tists as Lacassagne, Lomholt and others, who showed the distribution of heavy radioactive elements in tissue. Hamilton in California revived the technique in 1940 with his studies of the relationship of I^{131} to the thyroid gland. Particularly fruitful were the studies of Leblond, Gross and Bélanger of Canada, which contributed considerably to methodology and to knowledge of the normal function of the thyroid gland. Boyd, of the University of Rochester and Levi, of Copenhagen indicated the cellular possibilities of autoradiography by using C^{14} , the isotope of the biologically ubiquitous element carbon and showed that beta particles of C^{14} coming from a liver cell could be identified in photographic emulsion. Doniach and Pelc in England made the most significant advance in technique when they developed a thin photographic film emulsion that fa-

Department of Pathology, College of Medicine, State University of New York, Downstate Medical Center, Brooklyn, New York.

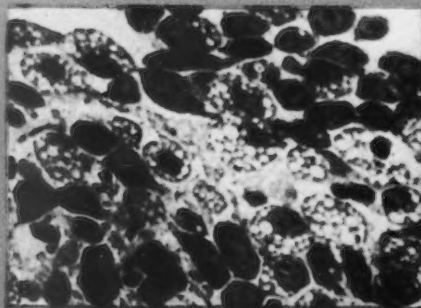
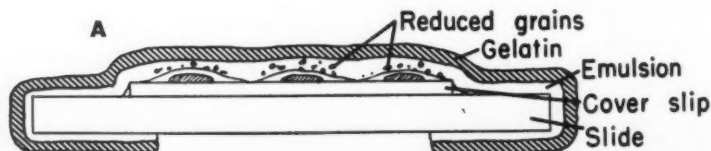
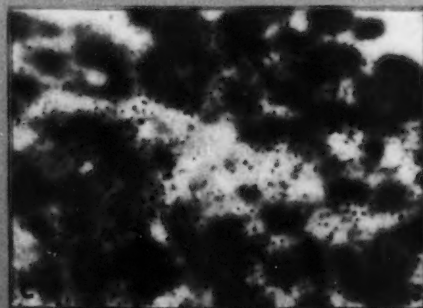


Fig. 1. Autoradiogram of tissue culture of a mouse sarcoma. Tissue culture cells were grown in a medium containing C^{14} -labeled adenine (a nucleic acid precursor). Histologic sections of tissue culture cells were covered with a photographic emulsion (A) and thus radioactive beta particles emanating from



the C^{14} -adenine incorporated in the cells produced silver grains in the emulsion. The microscopist focuses on the cell for morphologic studies (B) and then focuses on the overlying emulsion (C) to see any evidence of radioactivity coming from the underlying cell. ($\times 450$)

cilitated the ability to see the cellular concentration of the isotope. The Sloan-Kettering group introduced in 1951 the isotope tritium (H^3), which brings resolution to the intracellular level so that different concentrations of isotope in large chromosomes may be recognized. Most recently Hughes and his collaborators at the Brookhaven National Laboratory have used tritiated thymidine in an intensive and very important study of deoxyribonucleic acid (DNA) metabolism.

The localization of bone-seeking products of atomic fission, such as strontium (Sr^{90}), radiation changes and radiation-induced carcinogenesis in bone, have been reported by Vaughan and Lamerton of England and Hamilton, Arnold and Lisco of the United States. The effects of radiation on the hematopoietic system have been extensively studied by Cronkite at Brookhaven and Lajtha at Oxford.

The P^{32} , shown to be incorporated into regenerating liver tissue by counting techniques, may be further localized by autoradiography to individual cell types, e.g., liver parenchymal, bile duct, portal area, reticuloendothelial or vascular endothelial cells. In the study of the relative incorporation of nucleic acid precursors into cancer and control embryonic skin in tissue culture containing C^{14} -labelled nucleic acid precursors, it was proved that the cancer tissue incorporated much more than did the normal control cells. (Fig. 1.)

Pelc has shown that DNA is synthesized during the interphase of the cell mitotic cycle. Nucleic acid metabolism during irradiation has been investigated.

Autography, as in Fig. 2, revealed that the I^{131} taken up by the thyroid gland concentrated more in normal tissue than in the cancer. Several clinical studies have related the concentration of I^{131} to the morphology of thyroid cancer and have shown that the more colloid present the greater the uptake of I^{131} . Such studies have been of aid to the clinician by providing a cellular level of understanding for his isotope uptake and excretion studies, by suggesting reasons for the clinical response, or lack of response of thyroid cancer to I^{131} and by guiding the surgeon in the selection of thyroid nodules to be biopsied—"cold" ones being more likely to be malignant.

An intriguing and important study, recently, has been the application of tritiated thymidine autoradiography to a study of the genetic mechanism by Taylor at Columbia and by the Brookhaven group. Information concerning the structure of DNA and the genetic mechanism of replication has accrued from these studies. It is believed that the carcinogenesis problem and many other phases of cellular metabolism of normal and malignant tissues might be investigated profitably by this relatively simple, inexpensive and reliable technique.

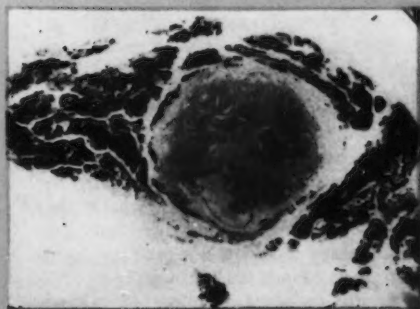


Fig. 2. Autoradiogram of a tissue section of a thyroid lobe from a patient with thyroid cancer who had been given radioactive iodine (I^{131}). The large, circular, lighter area is papillary cancer which does not concentrate significant amounts of I^{131} in comparison to the surrounding normal thyroid. ($\times 450$)

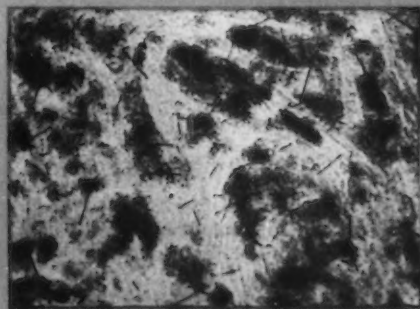


Fig. 3. Autoradiogram of a biopsy specimen of the liver from a jaundiced patient given thiosulfate twenty years before operation. The unoperated liver tissue is covered with a photographic emulsion that shows alpha particle tracks (thin straight lines) coming from large dark areas. ($\times 450$)

CANCER CLINIC



Combined Medical Radiotherapy Clinical Conference

Conducted by J. J. Nickson, M.D., and A. S. Glicksman, M.D.

For the past three and one-half years it has been the practice at Memorial Center to have a medical consultant in the Department of Radiotherapy. An attending radiotherapist and the medical consultant

jointly conduct rounds daily on all ward patients who are immediately under the care of the Radiotherapy Department, that is, assigned to one of their ward beds. The radiotherapy residents are required to attend these rounds twice a week.

*Departments of Medicine and Radiation Therapy,
Memorial Center for Cancer and Allied Diseases,
New York, N. Y.*

Approximately two thirds of the patients admitted to James Ewing Hospital

with a diagnosis of cancer have an associated medical problem. A recent study on 950 consecutive admissions revealed that one third of the patients with malignant neoplasms had either overt diabetes or an aberration in carbohydrate metabolism. In a publication last year (see p. 147), this group discussed the common electrolyte disturbances in patients undergoing radiotherapy. It is the purpose of this conference to demonstrate three typical medicoradiotherapeutic problems that are to be found on this service at present.

Case 1. Mrs. R. K., a 44-year-old white female, was admitted to the radiotherapy service of the James Ewing Hospital on June 30, 1958 complaining of abdominal cramps, nausea, anorexia, marked lethargy, weakness and headache. Four and a half years ago the patient had a radical mastectomy for carcinoma of the right breast. No postoperative radiation therapy was given. A year and a half ago, the patient developed recurrences on the anterior chest wall and skeletal metastases and was advised to have a bilateral oophorectomy which was performed on January 1, 1957. Remission lasted nine months. With the recrudescence of the disease, meticcorten therapy was instituted. This appeared to produce another remission and in January, 1958 a bilateral adrenalectomy was performed. At that time the surgeons reported liver metastases seen through the peritoneum. Following the adrenalectomy, the patient was maintained on 75 mg. of cortisone daily by mouth. Two weeks prior to admission the patient was referred to the radiotherapy service for a course of radiation to the persistent, progressive disease in the anterior chest wall. The patient was started on betatron therapy with electron beam to the chest wall, to an area containing several skin metastases, the largest measuring 8 x 6 cm. A 15 x 15 cm. portal was used with an energy of 10.4 mev.

DR. NICKSON: The electron beam was chosen since by its use the underlying pulmonary and mediastinal structures would be spared. The electron beam differs qualitatively from X-ray beams in that the energy is not exponentially ab-

sorbed within the tissues but rather has a definite range. Thus only 10 per cent of the maximal energy was found at a depth of 5 cm. from the surface. The use of electron beams thus eliminates the complication of pulmonary fibroses seen after X-ray treatment for similar conditions.

DR. GLICKSMAN: Approximately four days prior to admission the patient felt rather weak; she lost her appetite and vomited on occasion. She did not recall whether the cortisone tablets which she took regularly were retained or regurgitated. Because of the progressive weakness, nausea, vomiting and abdominal cramps, the patient was admitted for evaluation and to continue her therapy as an in-patient. On admission, physical examination revealed a well developed, well nourished white female who appeared acutely ill. Blood pressure was 88/60, pulse 120, weak and thready, respirations, 24, and deep. The pertinent physical findings included the absence of the right breast and the presence of metastatic nodules on the anterior chest wall covering an area of 5 x 4 cm. The heart and lungs were normal, the liver was palpable one finger below the costal margin. There were no significant masses in the abdomen, there was a generalized diffuse tenderness but no specific area of intense pain, localization or rebound. The rectal and vaginal examinations were essentially negative. Neurological examination revealed a diminution in the deep tendon reflexes throughout. No pathologic reflexes were elicited. The pertinent laboratory determinations are given in Table I.

TABLE I

Date	BUN	Na	K	Cl	CO ₂	Hb	Hct
6/25/58	25.5	126	5.87	96	20	15.5	47
6/27/58	20.0	134	5.30	102	24	14.0	43
7/7/58	15.4	135	5.31	101	24	13.8	42

RESIDENT: This is a typical picture of adrenal insufficiency. Is adrenal insufficiency a common complication of radiation therapy?

DR. GLICKSMAN: This patient represents a fairly typical case of adrenal insufficiency.

When the radiotherapy was instituted the patient was placed under additional stress; however, since her own adrenals had been removed and she was completely dependent upon exogenous adrenocortical hormone she could not meet the additional demand, therefore she developed a relatively severe adrenal insufficiency. The clinical picture of marked weakness and gastrointestinal complaints is fairly characteristic of the syndrome and is seen in 90 per cent of the cases. The serum electrolytes adequately demonstrate the metabolic acidosis which develops in these cases. The low sodium and relatively high potassium are characteristic of the syndrome and occur because of an increased Na and Cl excretion and K retention. The slightly elevated blood urea nitrogen reflects a decrease in the glomerular filtration rate associated with the usual hemoconcentration of these patients.

This patient was started on replacement therapy intravenously and received 100 mg. of intravenous cortisone (solucortef) in 5 per cent glucose and saline. Within six hours after the infusion the patient felt considerably stronger, and nausea, vomiting and abdominal cramps had subsided. Her blood pressure rose to 110/80, pulse dropped to 100. Her hematocrit reading, however, fell only to 43. She was started on intramuscular injections of cortisone (150 mg. per day) but the intravenous cortisone and saline were continued. The patient was continued on intramuscular cortisone for approximately one week and then given 125 mg. by mouth until the completion of radiation therapy. Upon the completion of radiation therapy the cortisone was slowly decreased to her usual maintenance dose of 75 mg. per day.

The patient made an uneventful recovery and continued her radiotherapy. Twenty-four treatments were given in forty days to a total tumor dose of 5200 r. There was good response in terms of diminution of the ulcerated areas.

RESIDENT: Do you see many cases here of adrenal insufficiency owing to stress of therapy?

DR. GLICKSMAN: This is not an unusual or uncommon complication. We had the op-

portunity in the last three and a half years to observe approximately six such cases and an additional nine cases of adrenal exhaustion in breast cancer patients who had not had adrenalectomies. The important point is that radiation therapy adds an additional stress to the patient. Should the patient be an adrenalectomized or hypophysectomized patient increased maintenance dosage of cortisone is indicated.

In the other large group of patients who developed the syndrome, are those patients who have been subjected to surgical procedures, to bone pain from metastatic disease or to additional emotional stresses placed upon them by the realization of the nature of their illness. When radiotherapy is instituted these patients may not have adequate adrenal function to withstand the additional demands and may develop relative adrenal exhaustion. They must be started on exogenous cortisone if adequate radiation therapy is to be carried to the completion of the prescribed course.

RESIDENT: Do you feel that postoperative radiation therapy has proved worthwhile?

DR. NICKSON: The question of the "worthwhileness" of postoperative radiation therapy to the site of operation and regional nodes after radical mastectomy remains a puzzling one. Neilson's series, reported just after the war, indicated a slightly, but statistically significant, increased survival in those patients receiving postoperative irradiation over those not so treated. Many of the earlier and negative studies were associated with low doses to the chest wall and to the regional nodes, doses of the order of 1500 to 2000 r. A properly planned series, preferably with random assignment of patients to the radiation and nonradiation group with doses ranging around 4000 r to the regional nodes, needs to be studied before any definitive answer can be given to the value of routine postoperative radiation treatment. It seems to me that in institutions where the incidence of chest-wall recurrence is less than 15 per cent, little is to be gained by treatment of the chest wall. On the other hand, treatment of the regional

nodes usually deemed inaccessible, the internal mammary and the supraclavicular nodes, probably is worthwhile. The dose must be as large as possible to give maximal chance for arresting any cancer cells in these areas. Doses of the order of 4000 r to the supraclavicular nodes and to the internal mammary nodes in three and a half to four weeks would appear to be optimal and feasible at this time. The major question, of course, remains. If these regional nodes are involved, what is the likelihood that the disease has not already spread to other areas in the body? No firm answer can be given to this question. It would appear that only by doing a properly designed clinical investigation would it be possible to derive a practical answer.

RESIDENT: Do you think that conventional radical mastectomy will be superseded by simple mastectomy plus post-operative radiation?

DR. NICKSON: The relative merits of routine radical mastectomy for patients with primary carcinoma of the breast versus simple mastectomy and postmastectomy radiation of the contents of the axillary, supraclavicular and internal mammary spaces remain an active and stimulating question. There is no gainsaying the fact that the five- and ten-year survivals reported by McWhirter, using simple mastectomy plus radiation, compare very favorably with those reported from good centers relying primarily on radical mastectomy. There are great difficulties in analyzing these figures since the clinical classifications used in varying centers differ enough to make it uncertain that one is comparing like types of cases. Nevertheless, the over-all absolute survival of patients treated by the newer procedure appeared to be as good as, and possibly in some instances better than, that achieved with radical mastectomy.

It is not my view that an institution which today has the radical mastectomy well in hand should depart from this procedure unless it also has an active and competent department of radiology with a broad spectrum of equipment. The problem is one for the clinical investigative

centers to resolve and not one for the practitioner to adopt. It is not my feeling that standard and useful means of treatment of cancer should be abandoned until it is well established that the supplanting procedure is better than the older one.

Case 2. Mrs. A. K., a 47-year-old white female, was first seen at this institution approximately four months ago with a large fungating mass in the left breast. Two 3-cm. nodes were palpable in the axilla. Prior to admission to the hospital the patient was carefully evaluated as to her operability. A skeletal survey failed to reveal any bone metastases. Chest plate was within normal limits. Serum calcium and urinary calcium were normal. Serum alkaline phosphatase and BSP were similarly normal. Therefore, in May, 1958 a left radical mastectomy was performed. Nodes were positive at all levels. The patient made an uneventful recovery from the surgical procedure. However, four weeks following discharge from the hospital the patient was seen in the clinic complaining of headache, lethargy and double vision. Neurological consultation and lumbar puncture substantiated the clinical impression of intracranial metastases. Radiotherapy consultation was requested; after the patient was started on radiation therapy to the head she was transferred to the radiotherapy service. On admission to this service the significant physical findings included nystagmus, papilledema, a well healed left mastectomy scar, normal heart and lungs. The abdomen was flat and soft, the liver was palpable two fingers below the costal margin and tender. No other intra-abdominal mass or organomegaly was palpable. She still had adiadochokinesis and astereognosis. There were no sensory or reflex changes. Significant laboratory findings included: Blood urea nitrogen of 10 mg./100 ml.; bilirubin 1.2 mg./100 ml., BSP 47 per cent, alkaline phosphatase 12 units/100 ml., cephalin flocculation 2+, thymol turbidity 3.4 units, the prothrombin time was 15.8 seconds; total protein (gm./100 ml.) 7.5, albumin 4.2 gm., globulins 3.4, CO₂ was 18, chloride 100, sodium 134, potassium 5.1 mEq./L.

DR. NICKSON: The use of radiation for treatment of secondary intracranial involvement deserves some comment here. Over the past five to six years the department has explored the role of treatment of patients with neurological defects. We have come to the conclusion that routine irradiation of these patients is a worthwhile palliative measure. A favorable response is seen in approximately one half of these patients as judged by decrease in their neurological defects or return to a normal neurological status. The duration of this improvement is, of course, variable. The maximum recorded duration of improvement is 24 months. The minimum that we feel may be regarded as justifying treatment is four months. Another factor influencing decision to treat deserves mention. Many of these patients by virtue of their neurologic metastases are incontinent of urine and feces, and otherwise incapable of managing themselves. This then places a severe burden upon family, patient and society. Good palliation then relieves a threefold burden and converts a patient whose care is expensive to a patient who can usually manage by himself at home.

The neurologic examination prior to initiating treatment showed paresis of the third, fourth and sixth cranial nerves. Headache and diplopia were the chief complaints. Upon completion of treatment, headache had diminished but diplopia was still present. This is not uncommon since improvement of some, on occasion all, neurologic signs or symptoms occurs after completion of treatment. This is a very interesting and unusual case. The rapidity of onset of evidence of metastatic disease after a careful screening before the surgical procedure, makes one believe that this woman has a very aggressive tumor. While this is somewhat unusual, it does however fall within the normal characteristics for this disease.

RESIDENT: In retrospect, considering rapid onset of symptoms of metastatic disease following the operation, would it have been preferable not to have intervened surgically?

DR. GLICKSMAN: It is of some interest that some patients appear to live in equilibrium with their tumors, while in other patients the tumors appear to grow in an uncontrollable fashion. One cannot help but consider the possibility that there may be another group of people who have a natural mechanism to control their tumors to the point of making treatment unnecessary. If one understood the natural mechanisms in those patients who can control their own tumors it might prove of tremendous therapeutic importance.

This tumor-host relationship can be affected by various regimens, the fundamental aim of which would be to improve the patient's ability to handle the tumor. Thus, surgical excision attempts to remove the tumor, thereby making it unnecessary for the patient to handle the disease at all; radiotherapy attempts to destroy the neoplastic tissue. Chemotherapy similarly attempts to interfere with the metabolism of the tumor in such a way that it would be destroyed. Upon occasion any of these therapeutic modalities may shift the tumor-host relationship, not in favor of the patient, but rather in favor of the tumor. Thus very shortly after surgical intervention widespread metastases may become apparent. Similarly, following radiation therapy an occasional patient may develop recurrent disease solely in the area of prior irradiation. This may be the situation in this patient where the tumor-host relationship was altered in favor of the tumor.

RESIDENT: Must one assume that changes in hepatic function are due to metastatic disease?

DR. GLICKSMAN: One cannot assume that the liver pathology is absolutely due to metastatic disease, but, of course, this would be our first choice. However, other possibilities must be considered. This woman has been operated upon within the last three months. She has also had injections of various antibiotics and analgesics; she had two transfusions two months ago. The time element is just about right for hepatitis, i.e., homologous serum jaundice. Furthermore, one cannot overlook the

possibility that the patient was given a drug for her nausea and vomiting by her local physician which may prove to be hepatotoxic such as the chlorpromazine group of drugs. A further possibility is that the woman came in contact with infectious hepatitis. Before instituting definitive therapy for control of metastatic disease in the liver, it is therefore of primary importance to be certain of the diagnosis. There have not been any clear-cut studies to indicate that radiotherapy delivered to an infected liver would worsen the disease; but intuitively one would have to assume it would not do very much good, if indeed it did not cause some harm. On the other hand, if the liver disease were neoplastic in origin, a course of radiotherapy to the liver may prove of some palliative benefit.

The serum glutamic oxaloacetic transaminase (SGOT) level would be of great help in the differential diagnosis. In homologous serum jaundice as well as viral hepatitis (catarrhal jaundice), SGOT will be markedly elevated (sometimes as high as 5000). The serum pyruvic oxaloacetic transaminase and lactic acid dehydrogenase level, will similarly be elevated. These enzyme levels are only slightly elevated in metastatic disease to the liver. Another diagnostic aid would be a liver aspiration. Provided that the prothrombin, bleeding and clotting times are normal and an adequate platelet count is present this procedure can be done with relatively little risk to the patient. The morbidity and mortality rate for aspiration biopsy of the liver is less than 1/10th of 1 per cent. Considering the importance of the information this is a negligible risk that should be undertaken wherever feasible.

DR. NICKSON: The question of palliation of secondary metastases in the liver has also received attention over the past five or six years. A detailed account of our experiences is not possible here. It can be summarized by saying that where pain, nausea and vomiting are the dominant symptoms they can be relieved with 75 per cent probability by the use of radiation. Commonly we employ 2500 to 3000

r to the entire liver with 1 mev X-ray beam in about two weeks. Concomitant with the improvement in symptoms, improvement in some or all of the liver function studies may be seen. Duration of improvement is short and for this reason we do not advocate routine treatment of patients with hepatic metastases. However, for those patients in whom the involvement of this organ by cancer is incapacitating, treatment may be indicated.

Case 3. Mrs. E. P., a 46-year-old colored female, was seen for the first time at Memorial Center in February, 1958, at which time a carcinoma of the cervical stump was found. The patient was treated by intracavitary radium and external ionizing radiation. There was initial improvement in the findings on serial pelvic examination and on serial Papanicolaou study.

DR. NICKSON: The management of this condition radiologically is hampered by the lack of the body of the uterus as a holder for radium. This limits the value of intracavitary radium. The radiologist must place greater reliance upon his external treatment with X-ray beams. Commonly, it is not possible to deliver more than 4000 or 5000 r to point A with intracavitary sources, and this only if a small tandem can be inserted into the cervical canal. Since greater reliance has to be placed on the external treatment we prefer to give external treatment with supervoltage X-ray or gamma-ray beams, including the entire pelvis and posterior opposing fields rather than to use divided field techniques. Dose should be carried as high as possible, but seldom should the mid-plane dose for the external treatment be less than 5000 r. This, commonly, cannot be delivered in less than five weeks. In patients whose side effects are severe, the time must be increased. By utilizing careful radiologic management and by individualizing treatment to the patient's circumstance, survival figures have been reported which compare favorably with those for carcinoma of the cervix in the undisturbed pelvis.

RESIDENT: At her last clinic appearance the patient complained of headache, puffiness of the face, nausea, anorexia and an-

uria of 36 hours' duration. Pertinent physical findings included blood pressure 210/120, 2+ papilledema, marked periorbital swelling, distended neck vessels, wet bilateral rales, heart enlarged to the left with a soft, systolic, apical murmur, liver palpable one finger below the costal margin. There was a grapefruit sized mass in the lower center abdomen. On pelvic examination there was a stony hard, fixed mass which was filling the pelvis and extended above the pelvic brim. There was 2+ pitting edema of the lower extremities. Hyperreflexia was also present. Catheterization yielded no urine.

TABLE II

Date	BUN	Na	K	Cl	CO ₂	pH	pCO ₂
4/2/58	15	145	4.43	106	25		
6/13/58	117	142	7.06	106	12	7.35	25
6/15/58	67	142	6.11	105	16		
6/19/58	31.2	136	4.85	97	24	7.41	42

DR. GLICKSMAN: This woman was obviously suffering from renal shutdown with renal acidosis. Although there was a slight possibility that this was due to a medical cause, e.g., chronic glomerulonephritis, lower nephron nephrosis or mercurial poisoning, the overwhelming evidence would favor ureteral obstruction because of tumor growth. Therefore, surgical consultation was requested for consideration of nephrostomy. Ureteral catheterization revealed bilateral obstruction. The patient was prepared medically by digitalization with 1.2 mg. of cedilanid intravenously. She was given 2000 cc. of 10 per cent invert sugar in water with 88 milliequivalents of sodium bicarbonate before operation.

After nephrostomy the patient required little intravenous alimentation because she could start eating almost immediately. Her appetite was good with little nausea and vomiting. In the first 48 hours following nephrostomy, the patient excreted between 3000 and 4000 cc. of urine per day. There was also a tremendous loss of electrolytes since the kidney had been damaged by the back pressure and could not retain salts, which it otherwise would be able to do. Thus in the immediate post-operative period, it was necessary to replace sodium bicarbonate and potassium.


The amount of fluid that was replaced was two thirds of the total loss. The BUN came down to normal within a week post-operatively.

DR. NICKSON: The whole question of treatment of recurrent carcinoma of the cervix is currently being reevaluated. The old position that these patients could not be helped following a definitive course of either surgery or radiation is probably not true. Our experience with patients recurrent after surgery would indicate that in a small selected group of patients, those with central recurrence unattached to the pelvic wall have a good chance of palliation or survival indefinitely, without reappearance of carcinoma of the cervix.

Some patients have survived from three to five years after proved surgical recurrence. The question of re-irradiation of radiation recurrence has been investigated by Murphy's group at the Roswell Park Memorial Hospital. In a similar class of patients, he has been able to show that re-irradiation does produce a small though definite probability of indefinite freedom from disease.

Brunschwig's study at Memorial Hospital has shown that operative procedures for carcinoma, recurrent after radiation or surgery provided that the lesion is centrally located, also have a good chance of palliation. Thus we see that thoughtful application of good surgical or good radiological techniques in selected patients has a good chance of palliation or even a small chance of cure, accepting the usual definitions of this term.

Medicine today is a fine mixture of art and science. No one individual can familiarize himself adequately with all the therapeutic disciplines necessary to treat adequately all patients. However, by the team work of individuals trained in the various disciplines in the management of each patient, it is possible within the scope of our present knowledge and abilities to give each patient the best of care. The cross pollination which occurs in these joint medical radiotherapy rounds, furthermore, serves a very useful purpose in the postgraduate education of our radiotherapy residents.



new developments in cancer

Tobacco a Cocarcinogen? . . .

In experiments at Columbia University, tars obtained from cigarettes burned at 500-700° F. failed to produce cancer when applied to the mouse skin. In combination with the common carcinogen, however, the tars produced significantly more papillomas and cancers than benzpyrene alone. In this role, tobacco tar proved to be more cocarcinogenic than is croton oil. The investigator, Dr. Alfred Gellhorn, offers the results as circumstantial evidence that air pollution and cigarette smoking may have synergistic or additive effects in producing lung cancer.

Sick Doctors . . .

Dr. C. E. McArthur of Olympia, Wash., Chairman of the American Medical Association's Section on General Practice, has disclosed the results of annual physical examinations given to doctors at the last three A. M. A. meetings. Of 3228 electrocardiograms, 18 per cent were definitely abnormal or borderline; of 2749 chest photofluorograms, 18 per cent showed suspected or definite abnormalities including tuberculosis, chest neoplasms and cardiovascular abnormalities. Among the reasons for the high cardiovascular death

rate among GP's, according to Dr. McArthur, are: nervous tension, insufficient exercise, inadequate or incorrect diets, long hours and resultant fatigue, failure to take vacations—and the physician's inattention to his own health.

Missing Enzymes . . .

Drs. V. A. Auerbach and H. A. Waisman of the University of Wisconsin have found that a number of important enzyme systems are missing in the highly malignant Novikoff rat hepatoma. Among the enzymes absent in the tumor were tryptophan peroxidase-oxidase, tyrosine transaminase, phenylalanine hydroxylase, threonine dehydrase, serine dehydrase, cysteine desulphydrase, histidase and *p*-hydroxyphenylpyruvic acid oxidase. The scientists have found that the livers of J leukemic rats also have defective enzyme systems.

Giant Cell . . .

A plastic human cell has been built and is on display at various medical meetings. It is big (12 feet high and 24 feet in diameter—or millions and millions times the size of the ordinary red cell); lifelike (built-in blue lights make it appear to

pulse) and as authentic as experts could make it. Each structure is labeled; and some of the basic chemistry of life is outlined in the cell's vast interior, which is capable of holding 40 people. Consultants on the project were Doctors K. Porter and M. Moses of the Rockefeller Institute, G. B. Wilson of Michigan State University, L. E. Roth of Argonne National Laboratory and H. W. Beams of the University of Iowa. The Upjohn Company had the cell built.

2-AAF Effect on Embryos . . .

A Rutgers investigator has tested 2-acetylaminofluorene (AAF) on the embryos of zebra fish and found that the well known rat liver carcinogen retarded both

growth and differentiation. After AAF treatment embryos, which were particularly sensitive to AAF during the early cleavage stage, developed edema of the pericardial and coelomic areas, cardiac failure and circulatory stasis, protuberances of the yolk mass, disorganization of the brain, spinal cord and sensory organs, deformities of the trunk and tail associated with abnormalities of the somatic musculature and notochord, cellular degeneration of the liver, epidermal hyperplasia and interference in melanin synthesis. The older the embryo, the more resistant it was to AAF. Dosage and duration of exposure were important factors in the damage wrought. The work was done by Dr. Kenneth Hisaoka, now at Loyola University, Chicago.

AMA on Voluntary vs. United Giving

The House of Delegates of the American Medical Association in June adopted the following resolution:

Whereas, The objectives of the principal Voluntary Health Agencies are laudable; and

Whereas, These agencies have a distinguished record of contribution to the health and medical care of the American people; and

Whereas, The House of Delegates in December 1957 expressed commendation of such agencies and adopted "Suggested Guides to Relationship between Medical Societies and Voluntary Health Agencies"; and

Whereas, It is recognized that the continued effectiveness of these organizations in the fields of public education, professional education and research is dependent upon the retention of their independence and identities; now therefore be it

Resolved, That the House of Delegates reiterate its commendation and approval of the principal Voluntary Health Agencies; and be it further

Resolved, That it is the firm belief of the American Medical Association that these agencies should be free to conduct their own campaigns of fund raising and public education and to direct programs of research in their particular spheres of interest; and be it further

Resolved, That the House of Delegates respectfully request that the American Medical Research Foundation take no action which would endanger the constructive activities of the Voluntary Health Agencies; and be it further

Resolved, That the Board of Trustees continue actively its studies of these perplexing problems looking forward to their ultimate solution.

pain is present -- not every six hours; don't avoid the patient because you can still treat the mind and spirit. One of the physician's greatest satisfactions comes from still trying to help the hopeless patient. Karnofsky also issued a plea to physicians to continue to administer to the terminal patient. The patient should be studied right up to the end to learn more about the disease; while the problem may be different in smaller centers with limited hospital facilities, the practice in larger centers is to prolong life, even in the dying patient, as long as possible; if the physician becomes tired and passive, it may be a good idea to call in another physician for a fresh evaluation of the patient and the disease. Miller asserted that a mother with advanced cancer should be permitted to do whatever housework she can; these patients don't like another woman to run their homes if it can be helped. Jewett said he never volunteers information that the patient has cancer except to a responsible member of the family; if the patient insists strongly on knowing, however, he may tell the patient; the two principal sources of psychological support for patients are religion and the physician. Attending the advanced and dying patient may be a heart-rending experience for any physician -- but it may be well to remember that the physician himself someday may be on the receiving end. In response to a complaint about publicizing the symptoms and need for early diagnosis and treatment, one physician said: "Cancerophobia is a horrid disease -- but it doesn't metastasize."

A transmissible factor, which drastically reduces rat resistance to dye-induced hepatoma, has been reported by Richardson (U. of Wash.) and Griffin and O'Neal (M. D. Anderson). Normally 2 per cent of Sprague-Dawley rats showed hepatomas after prolonged feeding with 3'MeDAB. After being housed in the same room with Long-Evans rats (with a high hepatoma rate), as much as 20 per cent of the S-D's produced hepatomas. The longer the S-D's and L-E's were neighbors, the higher the S-D hepatoma incidence. Bennett (U. of Wash.) said the statistics on more than 1500 rats in these series were highly significant -- "in less than one case in a thousand could this result be attributed to chance."

The Berliners and Dougherty (U. of Utah) have reported that each kind of cancer they have examined so far has a distinctive chemical personality. Exquisite radio-

chromatographic methods show that each type of cancer handles cortisol in a different manner. Some tumors yielded about ten cortisol metabolites, a few of them new to the investigators. Among the tumors tested were mouse leukemia, lymphosarcoma, fibrosarcoma, breast carcinoma and tumors of the salivary gland, dog osteosarcoma and human leukemia. Normal tissues yielded different and predictable cortisol products.

Barach, Beck and Bickerman (Columbia-Presbyterian, New York City) reported at the A.M.A. annual meeting they have developed a self-propelled, hand-sized nebulizer with an inexpensive, built-in heater thermostat which warms a salt spray -- sprayed into the bronchi, the solution makes a patient cough up sputum for lung cancer detection purposes.

Santos and Sweet (U. of Mich.) recommend balanced analgesia (anesthesia minus true hypnosis) for poor-risk thoracic surgery patients. Increasing within safe limits the concentration of nitrous oxide and meperidine to control signs of inadequate analgesia is preferable to a relaxant. Patients so treated have a short and relatively uncomplicated postoperative course and no memory of pain during partial analgesia.

Raskin, Kirsner and Palmer of Chicago report finding cytologically: 66 of 69 esophageal carcinomas; 125 of 131 stomach carcinomas and lymphomas (plus four false positives); 25 of 42 carcinomas of the pancreas; four of eight malignant neoplasms of the biliary tract; four carcinomas of the duodenum; 36 of 38 cancers of the colon too high for proctoscopy.

Buckwalter, Soper and Knowler of Iowa City examined serum from 2370 psychotics, 566 patients with intracranial lesions and 49,979 volunteer blood donors and found statistically increased incidences of psychosis among blood type O and of intracranial neoplasms among blood type A individuals.

Steiner (U. of Chicago) reviewed 2000 post mortems at General Hospital, Lagos, Nigeria, and reported in Cancer Research: 11 per cent had reached age 50 or more; only 5.6 per cent had malignant tumors; and 23 per cent of all cancers were of the liver.

Berger, Kremens and Gershon-Cohen of Philadelphia state that in the routine X-ray examination of the female breast, a diagnosis can be made in about 75 per cent of all cases.

COMING MEDICAL MEETINGS

Date 1958	Meeting	City
Oct. 13-15	Association of American Medical Colleges	Swampscott, Mass.
Oct. 13-15	National Rehabilitation Association	Asheville, N. C.
Oct. 13-17	Postgraduate Week, New York Academy of Medicine. <i>Research Contributions to Clinical Practice</i>	New York City
Oct. 20-21	Scientific Meeting, American Cancer Society. <i>Symposium on Cancer of Colon and Rectum</i>	New York City
Oct. 20-23	American College of Gastroenterology	New Orleans
Oct. 20-23	American Academy of Pediatrics	Chicago
Oct. 21-23	American Dietetic Association	Philadelphia
Oct. 24-26	American Heart Association	San Francisco
Oct. 27-31	American Public Health Association	St. Louis
Oct. 28-31	Iowa Nurses' Association	Mason City, Iowa
Nov. 2-8	Inter-American Congress of Radiology	Lima, Peru
Nov. 3-6	Southern Medical Association	New Orleans
Nov. 3-7	American Society of Clinical Pathologists	Chicago
Nov. 3-8	College of American Pathologists	Chicago
Nov. 4-6	New England Postgraduate Assembly	Boston
Nov. 4-8	American Society of Tropical Medicine and Hygiene	Miami Beach
Nov. 6-8	Gerontological Society	Philadelphia
Nov. 10-13	American Dental Association	Dallas
Nov. 10-13	Interstate Postgraduate Medical Association of North America	Cleveland
Nov. 13-15	Annual Scientific Meeting, Inter-Society Cytology Council	New York City
Nov. 16-21	Radiological Society of North America	Chicago
Nov. 17-19	Association of Military Surgeons of the United States	Washington, D. C.
Nov. 18-20	National Conference on Air Pollution	Washington, D. C.
Nov. 20-22	American College of Cardiology	New Orleans
Dec. 2-5	American Medical Association	Minneapolis
Dec. 6-11	American Academy of Dermatology & Syphilology	Chicago
Dec. 15-19	Second Australian Conference in Radiation Biology	Melbourne

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